A Dissertation on

A STUDY OF SERUM ALBUMIN LEVEL AS A PROGNOSTIC INDICATOR OF ACUTE ISCHEMIC STROKE

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With partial fulfillment of the regulations for the award of the degree of

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I solemnly declare that this dissertation entitled **"A STUDY OF SERUM ALBUMIN LEVEL AS A PROGNOSTIC INDICATOR OF ACUTE ISCHEMIC STROKE"** is a bonafide and genuine research work carried out by me at Coimbatore Medical College and Hospital during the academic year 2016 -2019 under the guidance and supervision of **Dr.Kumar Natarajan M.D**, Professor, Department of Medicine, Coimbatore Medical College Hospital, Coimbatore.

This dissertation is submitted to The Tamil Nadu Dr.M.G.R Medical University, towards the partial fulfillment of requirement for the award of M.D. Degree in General Medicine (Branch -I).

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Dr. AAKASH CHOZAKADE

ABBREVIATIONS

ACA- ANTERIOR CEREBRAL ARTERY

CAD- CORONARY ARTERY DISEASE

CT-COMPUTED TOMOGRAPHY

DM-DIABETES MELLITUS

ECG-ELECTROCARDIOGRAM

GCS-GLASGOW COMA SCALE

MCA-MIDDLE CEREBRAL ARTERY

MRI-MAGNETIC RESONANCE IMAGING

MRS-MODIFIED RANKIN SCALE

PCA- POSTERIOR CEREBRAL ARTERY

PET- POSITRON IMAGING TOMOGRAPHY

SHT-SYSTEMIC HYPERTENSION

SSS-SCANDINAVIAN STROKE SCALE

TRANSIENT ISCHEMIC ATTACK

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INTRODUCTION

Stroke is one of the major causes of mortality and morbidity worldwide. After coronary artery disease and cancers of all types, stroke is the third commonest cause of death worldwide.

The World Health Organisation (WHO) defines stroke as rapid development of clinical signs and symptoms of a focal neurological disturbance lasting more than 24 hours or leading to death with no apparent cause other than vascular origin (WHO 2015).

In India, age adjusted prevalence rate of ischemic stroke is 250-350/1,00,000 and stroke contributes 1.2% of total death in India. As late as 2000, India was ranked among countries lacking sufficient data on stroke.

Over 80% of death due to stroke occurs in low-income and middle-income regions of the world. Identifying predictors of mortality is important so that prompt therapeutic measures could be initiated to improve outcome.

Early mortality due to stroke is directly related to stroke. Complications affect the mortality only later in the course .Previous studies have elucidated the various risk factors of stroke as well as the factors which influence mortality, which serve as predictors of mortality. Stroke severity, type of stroke, increased age, level of consciousness and hyperglycaemia are a few of them. These are non-modifiable, hence of limited interest in clinical practise.

Identification of predictors of mortality which are modifiable are vital so that prompt therapeutic measures can be started to improve outcome.

Albumin is a multi-factorial protein which has been proven to have neuroprotective effect in animal studies. Albumin also is an indicator of nutritional status.

Studies on prognostic factors of ischemic stroke in our population are limited. Serum albumin level at admission was found to be an independent prognostic factor for ischemic stroke outcome in studies done in western population. Some of the studies have shown that albumin transfusion is capable of minimising volume of infarction and cerebral edema. Albumin reduces the hematocrit as well as the erythrocyte sedimentation rate by its affect on erythrocyte aggregation. Effect of albumin is primarily in the early reperfusion phase of acute ischemic stroke where it has an inhibitory effect on thrombosis, stagnation and adhesion of leucocytes in microcirculation.

There is scarcity of data regarding the usefulness of albumin as a prognostic indicator. Hence through this study, the goal is the understand the association between serum albumin on admission and the functional status at 90 days. It also aims to find the other indicators that influence the outcome after ischemic stroke.

AIMS AND OBJECTIVE

1. To study whether serum albumin is a good prognostic indicator of acute ischemic stroke using modified rankin scale at 3 months follow up of patients admitted in general medicine ward, Coimbatore Medical College Hospital

2. To identify other clinical and biochemical factors affecting the prognosis of acute ischemic stroke as measured by modified rankin scale at 3 months follow up

3. To measure the stroke severity at admission using scandinavian stroke scale.

REVIEW OF LITERATURE

Human brain composed of 100 billion neurons forming trillions of connection with other brain cells, making it one of the most complex structures. The integrative power of the brain is the result of the integrity of these connections. Stroke is one disease that has helped us understand the brain in greater detail. Different symptoms that occur after a stroke signify the different areas that are affected. The disability caused by stroke is because of the inability of the brain cells to regenerate.

Globally about 15 million new stroke events occur every year, two-third of which occur in people living in low income and middle income countries. Demographic transition resulting from adaptation of westernized lifestyle is also likely to increase the burden of stroke in developing economies [1].

Ischemic brain stroke is caused by sudden cessation of blood supply to the brain, resulting in corresponding neuronal cell death and neurological loss of function.[1] Acute Ischemic stroke (AIS) is caused either by a thrombus or an embolus resulting in complete occlusion of cerebral vessel. Occlusion and vascular cessation damages the concerned brain areas.[1,2] AIS is more common than the hemorrhagic brain stroke. Brain stroke is a cause of morbidity and mortality. WHO estimates show the brain stroke is second most leading cause of mortality next to the ischemic heart disease in the developed countries, whereas in poor countries it ranks sixth leading cause.[2] It is crucial

to diagnose the acute brain stroke at the earliest as the available drug therapy reduces the morbidity and mortality and improves the patient prognosis.

ANATOMY

All the arteries supplying the brain are branches of the brachiocephalic arteries arising from the aorta. The common carotid arteries of both sides ascend the anterior neck and bifurcate at the level of the angle of mandible forming internal and external carotid arteries. The internal carotid artery with its tributaries, the middle cerebral artery(MCA) and anterior cerebral artery(ACA) forms the anterior circulation which perfuse the entire frontal and parietal lobes and most part of temporal lobes.

Posterior circulation (vertebrobasilar system) is formed form the right and left vertebral arteries which are branches of the subclavian artery arising from the aorta. They ascend within the vertebral foramen and loop over the transverse process of C1 vertebra and enter the skull via foramen magnum. The vertebral arteries of both side join to form basilar artery at the level of pons. Basilar artery bifurcates at the level of midbrain forming the right and left posterior cerebral artery. The vertebrobasilar system with its perforating branches perfuse the brain stem , cerebellum, thalamus, occipital lobe and part of temporal lobe.

At the base of brain, the major arteries meet to form the Circle Of Willis where the anterior cerebral artery and the middle cerebral artery are linked to the posterior cerebral artery by anterior and posterior communicating artery.

The anastomosis forms the communication between the anterior and the posterior circulation, and between the right and left side of the brain.

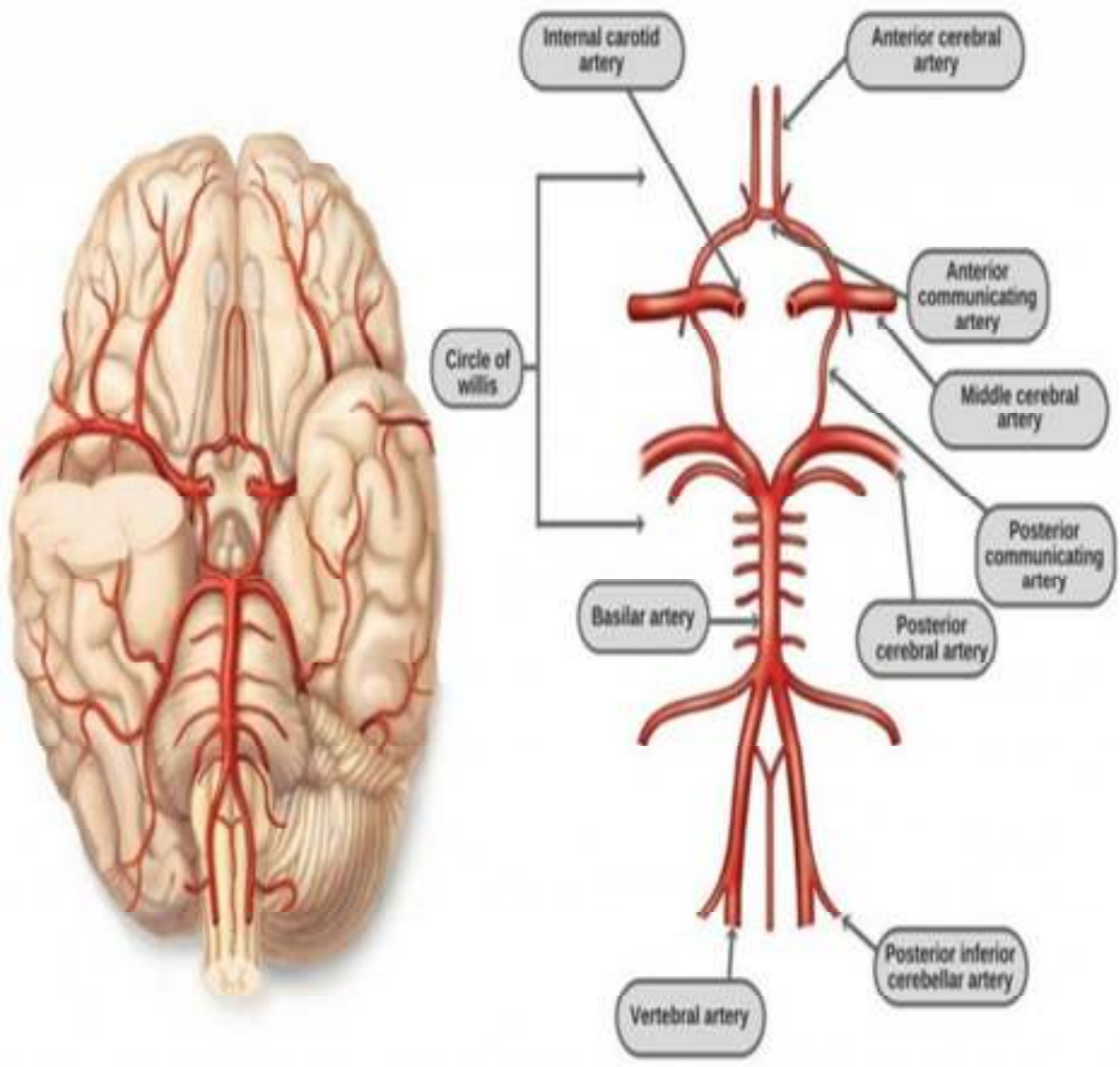


FIGURE NO. 1- ARTERIAL SUPPLY OF BRAIN: CIRCLE OF WILLIS

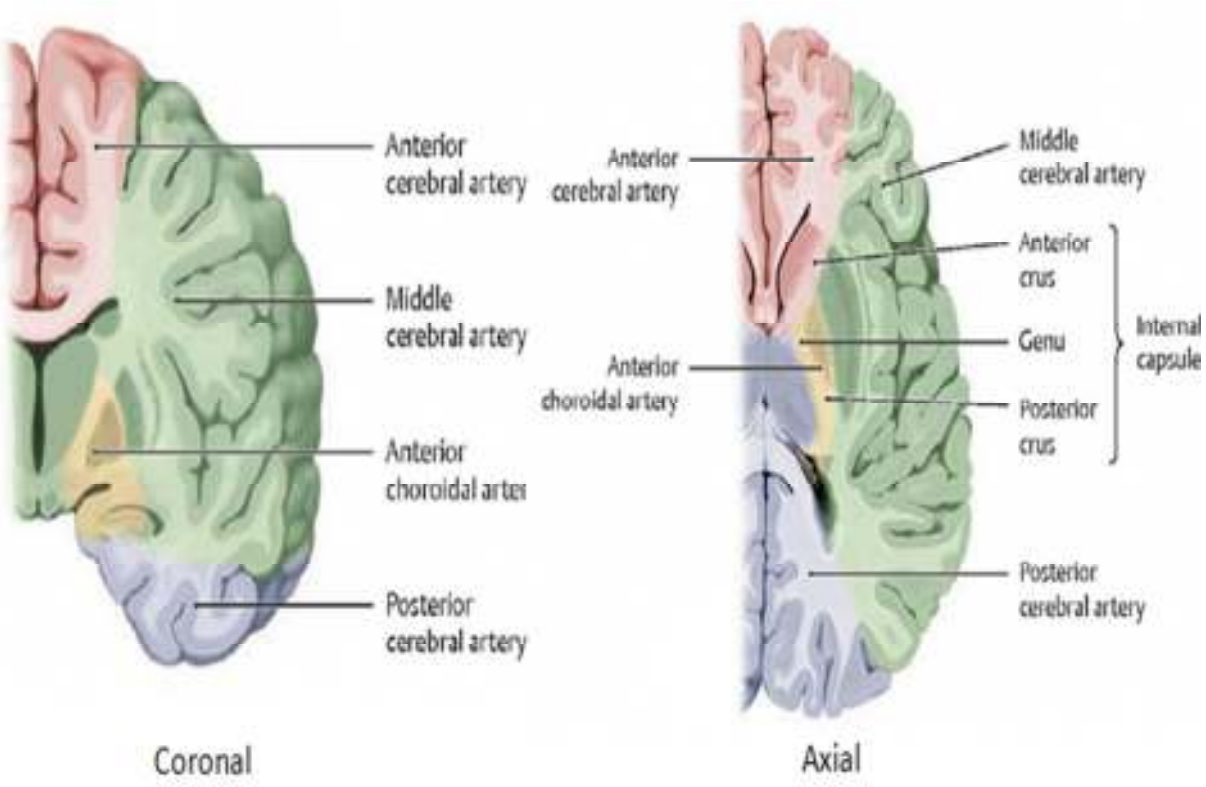


FIGURE NO.2- VASCULAR TERRITORIES OF THE BRAIN

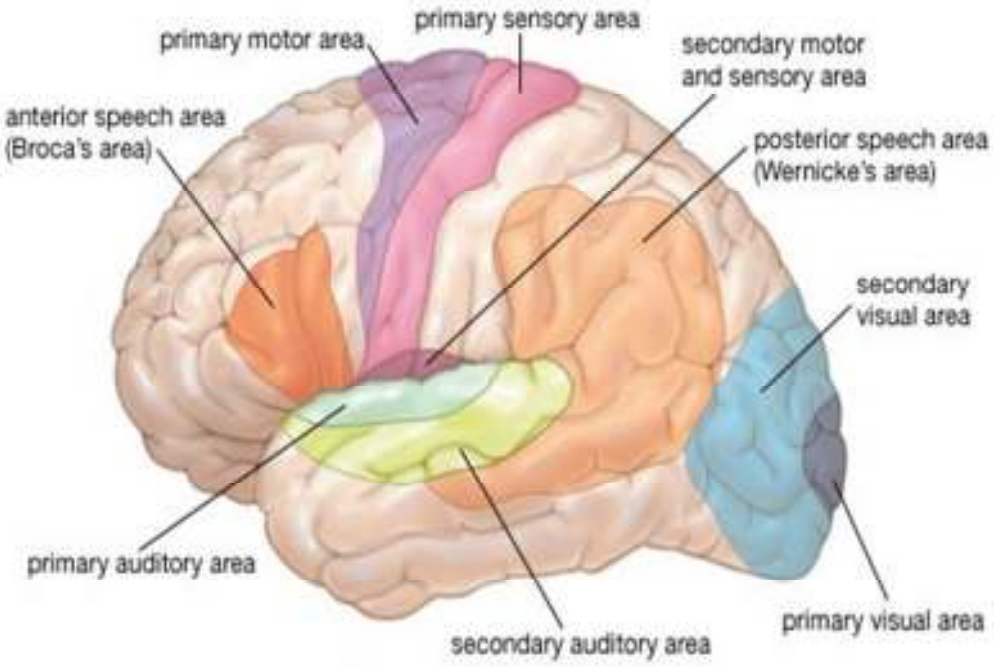


FIGURE NO.3- FUNCTIONAL AREAS OF THE BRAIN

WHO definition of stroke

Rapidly developing clinical symptoms or signs of focal or global loss of cerebral function with symptoms lasting for more than 24 hours or leading to death with no apparent cause other than vascular origin.

TYPES OF STROKE

- ISCHEMIC -85%
- HEMORRHAGIC- 15%

HEMORRHAGIC STROKE

TYPES

- Subdural / Epidural Hemorrhage: produced by trauma
- Subarachnoid hemorrhage-: due to trauma or rupture of intracranial aneurysm
- Intraparenchymal hemorrhage

INTAPARENCHYMAL HEMORRHAGE

- Most common type: intracerebral hemorrhage
- Causes
    - Hypertension
    - Trauma

- Cerebral amyloid amgiopathy
- Cocaine and amphetamine use(in young)
- Coagulopathy
- AV malformation
- Metastatic brain tumour

ISCHEMIC STROKE

ETIOLOGY

- Thrombosis
  - Large vessel thrombosis
  - Lacunar(small vessel) stroke
  - Dehydration
- Embolic occlusion
  - Artery to artery
    - Carotid bifurcation
    - Aortic arch
    - Arterial dissection
  - Cardioembolic

- Atrial fibrillation
- Mural thrombus
- Myocardial infarction
- Dilated cardiomyopathy
- Valvular lesion: mitral stenosis

  Mechanical valve

  Infective endocarditis

- Paradoxical embolus: Atrial septal defect

  Patent foramen ovale

- Atrial septal aneurysm
- Spontaneous echo contrast

PATHOPHYSIOLOGY OF ISCHEMIC STROKE

CEREBRAL BLOOD FLOW

- Normal cerebral perfusion is about 50-60ml/ 100gm /min[15]

  Since neurons are incapable of anaerobic respiration, and the absence of stored glucose ,the effects of brain ischemia are rapid . In response to ischemia, vascular autoregulatory mechanisms come into play by local vasodilatation, opening of collaterals and increased utilisation of oxygen and glucose from blood.

- A decrease in cerebral perfusion to zero leads to death of brain tissue within 4-10 min.

- Reduction to less than 10ml/100gm/min of brain tissue culminates in irreversible neuronal injury.

- A decrease to less than about 16-18ml/100gm/min results in infarction within an hour.

- When blood flow decreases to less than 20ml/100gm/min, an electrical silence ensues with a reduction in synaptic activity to preserve energy stores. This results in ischemia without infarction, unless this situation is extended for several hours or days[16].

If reperfusion occurs before significant amount of cell death, there maybe only transient symptoms ,and this is referred to as transient ischemic attack(TIA). The definition of TIA requires all the neurological signs and symptoms to resolve within 24 hours regardless of whether there is imaging evidence of new permanent brain injury[15].

Syncope ensues due to a generalised reduction in cerebral blood flow due to systemic hypotension. If the reduced blood flow persists longer, infarction develops in the border zone of major arterial territories. Severe global hypoxia ischemia causes extensive brain damage referred to as hypoxic ischemic encephalopathy(HIE).[15]

FOCAL ISCHEMIC INJURY

Vascular occlusion due to thrombus or embolus can lead to ischemia of the affected vascular territory. At gross tissue level, vascular compromise leads to acute ischemia or infarction which is a dynamic process evolving over a period of time. At cellular level, hypoxia leads to neuronal injury.

NEURONAL INJURY

Ischemia triggers activation of destructive vasoactive enzymes released by the endothelium, leucocytes, platelets and other neuronal cells which promote the formation of microthrombus which causes occlusion in the cerebral microcirculation[17].

At molecular level, hypoxic ischemic neuronal injury is mainly brought about by the overaction of neurotransmitters – glutamate and aspartate. This process is called excitotoxicity[18]. Its onset is triggered by depletion of cellular energy stores. Glutamate is normally stored in the synaptic terminals. It is cleared from the extracellular space. This causes the opening of calcium channels associated with

N-Methyl-D-Aspartate (NMDA) and Alpha- Amino-3-Hydroxy-5-methyl-4-Isoxanole propionate (AMPA) receptors. Persistent membrane depolarization causes influx of calcium, sodium and chloride ions and efflux of potassium ions[19]. Increase in the intracellular calcium induces activation of destructive enzymes like proteases, lipases and endonucleases. These cause the release of cytokines and other mediators which ends up destroying the cellular integrity[20].

Inflammatory response to tissue damage is mediated by various inflammatory mediators , Tumour Necrosis Factor being the key agent. Leucocyte recruitment to the ischemic areas occurs within 30 minutes of ischemia and reperfusion. Leucocytes cause the activation of vasoactive substances like oxygen free radicals, arachidonic acid metabolites (cytokines) and nitric acid. These cause vasodilatation, vasoconstriction, increased permeability, enhanced platelet aggregation, increased leucocyte adhesion to the endothelial wall and immune-regulation.

First to respond to hypoxia are endothelial cells. The response is morphological, biochemical as well as immunological causing varied physiological and pharmacological effects. Endothelial cells swell and form microvilli on their luminal surface-this causes a narrowing of luminal patency of capillary vessels. As a result, mechanical plugging of the capillaries by erythrocytes, leucocytes and platelets ensues[21].

Endothelial cells mediate the action of vasoactive agents like endothelin, peptides, eicosanoids; and smooth muscle relaxants such as nitric acid. These agents alter the vascular tone of the microcirculation. The key step in the initiation of the inflammatory process, leucocyte adherence to the endothelial wall, is brought about by activation of endothelial adhesion molecules.

ISCHEMIC PENUMBRA

Within about an hour of hypoxic ischemic insult, an oligemic region called ischemic penumbra develops around a central core of infarction, where the autoregulation is ineffective. In this area, cellular integrity and some amount of energy metabolism is preserved. Neurological deficits due to worsening of ischemia in this region can be partially or fully reverted by reperfusing within a critical time period (2-4hrs) called the Window Of Opportunity[22].

Pathophysiology of the ischemic penumbra is closely related to generation of Spontaneous Waves of Depolarisation (SWD). These are multifocal in origin, some arising from the core of infarction, and some from the ischemic penumbra. They are associated with sustained increase in synaptic glutamate and extracellular potassium[23]. Hypoxic/ rapid depolarisations of the neuron supervene just before irreversible neuronal death.

NEURONAL DEATH

Occurs by 2 processes-

Coagulation necrosis

Apoptosis

Apoptotic mechanisms start within an hour of ischemic injury whereas necrosis sets in about 6hours after arterial occlusion.

Coagulation Necrosis

Rapid breakdown of the cellular cytoskeleton primarily due to energy failure. due to effects of physical, chemical and osmotic damage to plasma membrane. Cell initially swells, then shrinks and undergoes pyknosis over 6-12hrs. By 24hours, extensive chromolysis has occured resulting in pannecrosis. Astrocytes swell and fragment, myelin sheath degenerates[16].

Apoptosis

This is programmed cell death. Nuclear damage is the first one to occur. Integrity of the plasma membrane and mitochondrial membrane are preserved till the end. Prolonged ischemia causes activation of latent suicide proteins in the nucleus which triggers the autolytic processes causing cell death. This autolytic process involves DNA cleavage[24].

Ischemia leads to starvation of the neuron due to lack of glucose and oxygen leading on to failure of mitochondria to produce ATP. In the absence of energy in the form of ATP, membrane ion pumps stop functioning causing depolarisation of neurons and increase in the intracellular calcium. Cellular depolarisation also causes increased release of glutamate from the synaptic terminals. Excess glutamate activates postsynaptic receptors which enhance the neuronal calcium influx resulting in neurotoxicity. Free radicals formed by lipid degradation and mitochondrial dysfunction result in catalytic destruction of the membrane and damage other vital cell functions.

Progression and extend of ischemic injury in stroke depends on[25]

- Rate of progression and onset- short duration and slow onset strokes are better tolerated
- Collateral circulation- good collateral circulation around the ischemic area coorelates with better outcome

- Systemic circulation- constant cerebral perfusion pressure depends on adequate systemic blood pressure
- Haematological factors- hypercoagulability causes exacerbation of the vascular occlusion by increasing the progression and extend of thrombus.
- Temperature- increased temperature worsens the ischemic injury
- Glucose metabolism- hyperglycemia adversely affects size of the infarct

SUBCLASSIFICTION OF ISCHEMIC STROKE

LARGE VESSEL ATHEROTHROMBOSIS

Involves both intracranial and extracranial arteries.

Atherosclerosis is the most common pathology underlying vascular occlusion causing thrombotic stroke[26]. There is formation of lipid-rich atherosclerotic plaques on the inner wall of large vessels.

They form over a prolonged time course with the effect that the brain is able to adjust to the gradual reduction in cerebral blood flow[27]. Infarcts occur only when a critical level of stenosis is reached. These atherosclerotic plaques are susceptible to ulceration, thrombosis, calcification, and intraplaque hemorrhage and the susceptibility depends on the structure, composition and consistency[28]. Depending on the vessels involved, location of the lesion within the affected vessel, rapidity of development and the presence or absence of

anastomoses around the area, it typically ends up in single large territorial stroke.

Most common sites

- Bifurcation of common carotid artery[29]
- Origin of vertebral artery
- Course of middle cerebral artery prior to bifurcation

Risk factors- hypertension

Diabetes mellitus

Dyslipidemia

EMBOLIC STROKE

- usually sudden in onset with maximum neurological deficit at the onset
- Non- rheumatic atrial fibrillation is the most common cause of cerebral embolism overall, the risk of which is calculated by using CHA2DS2VASc score.

CARDIOEMBOLIC STROKE

- Occur sue to embolism of thrombotic material on the atrial, ventricular or left heart valves.

- They usually occur in more than one arterial distribution, mostly anterior circulation[30].
- Acute strokes involving the right and left anterior circulation are considered embolic unless proven otherwise[31].
- The location and extend of the infarct depends on the extend of collateral circulation.
- The most common causes of cardioembolic stroke are non-rheumatic/non valvular atrial fibrillation, myocardial infarction, prosthetic valves, rheumatic heart disease, and ischemic cardiomyopathy.
- In paradoxical embolism, a venous thrombus migrates into arterial circulation through an atrial septal defect or a patent foramen ovale.
- Other than venous clot- fat emboli, tumour emboli, bacterial endocarditis, intravenous air and amniotic fluid emboli can also cause paradoxical embolisation.

ARTERY TO ARTERY EMBOLIC STROKE

- Thrombus formed on the wall of a particular vessel fragments and sheds pieces of clots. These are swept downstream and may lodge in smaller branches of the large arteries causing multiple smaller clots within the territory of the smaller vessel[32].

- Most common cause of embolus- carotid bifurcation atherosclerosis

CAROTID ATHEROSCLEROSIS

- Most common sites- common carotid bifurcation

  Proximal internal carotid artery

- Risk factors- male gender

  Old age

  Smoking

  Hypertension

  Diabetes

  Hypercholesterolemia

- Classified based on degree of stenosis and whether stenosis is symptomatic or not.

INTRACRANIAL ATHEROSSCLEROSIS- produces stroke either by insitu thrombosis or embolism.

DISSECTION OF INTERNAL CAROTID OR VERTEBRAL ARTERIES-

- Trauma
- Spinal manipulation surgeries

- Ehlers danlos type 4
- Marfan' syndrome
- Cystic medial necrosis
- Fibromuscular dysplasia

Neurological outcome of and embolic stroke depends on the affected vascular territory and the tendency of the embolus to cause vasospasm by acting as a vascular infarct. Vasospasm tends to occur in young patients since the vessels are more pliable and less atherosclerotic[33].

Many embolic strokes become hemorrhagic resulting in HEMORRHAGIC INFARCT(RED INFARCT)[34] where bleed occurs into the necrotizing cerebral tissue. Pathogenesis of hemorrhagic infarct is explained by 2 mechanisms[35]

- Reperfusion of the ischemic tissue following spontaneous lysis of the embolus.
- In persistent occlusion of the vessel proximally, due to reperfusion from the leptomeningeal vessels that form the collateral circulation.

Probability of hemorrhagic infarction depends on the size of the infarct, extent of collateral circulation, and the use of anticoagulant and thrombolytic agents.

SMALL VESSEL STROKE

LACUNAR INFARCTION

- Caused by occlusion of small penetrating arteries
- Involves the 30-300 micrometer branches of the major cerebral arteries that penetrate into the deep gray and white matter of the brainstem or cerebellum.
- Occlusion by atherosclerotic disease or lipohyalinotic thickening
- Small infarcts 3mm to 2cm diameter causing lacunes
- Risk factors- Hypertension, age
- Pure motor stroke- 33 to 50% of all small vessel strokes
- A large vessel stroke may initially manifest as lacunar syndromes.

Lacunar syndromes referable to posterior circulation[31]

- Hemiballism
- Hemichorea
- Isolated dysarthria

GLOBAL ISCHEMIA/ HYPOTENSIVE STROKE

- Occurs following drastic reduction in systolic BP due to any cause.
- Cerebral gray matter is particularly vulnerable
- The more susceptible neurons are the Purkinje cell layer of hippocampus and Purkinje cell layer of the cerebellar cortex.
- Abundance of glutamate makes them more susceptible to global ischemia.
- Global ischemia causes maximum damage to areas between the territories of the major cerebral and cerebellar arteries called the 'Boundary zone' or 'Watershed Area'.

WATERSHED INFARCT

- Develops in the region between the adjacent arterial territories which share a collateral circulation.
- Parietotemperopccipital triangle at the junction of anterior, middle and posterior cerebral arteries is most common affected[36].
- Results in paralysis and sensory loss of the arm sparing the face and speech
- Comprises 10% of ischemic strokes
- 40% occur in carotid stenosis/occlusion

BORDERZONE/TERMINOTERMINAL INFARCTS[37]

Occurs between two arterial territories whose parent vessels do not share a collateral flow.

STROKE DUE TO UNDERTERMINED CAUSE

- Includes case where complete workup and screening for cardiac conduction/ structural abnormalities, intracranial/ extracranial large artery occlusions, coagulopathies and other underlying conditions has been inconclusive.
- Clinical situation where complete workup cannot be done is also included in this.
- Since they form a large share of strokes, newer sub classifications like ASCO and computer-aided SSS-TOAST have been proposed to study their outcomes and riskfactors[38].

CONDITIONS THAT MIMIC TIA/STROKE

- Migraine
- Seizure
- Hypoglycemia
- Brain tumor
- Arteriovenous malformation

- Multiple sclerosis
- Incipient syncope
- Orthostatic hypotension
- Cardiac arrhythmia
- Amnesia
- Narcolepsy/cataplexy
- Intracranial inflammation (Meningitis/Encephalitis)
- Periodic paralysis

Compressive neuropathy

- Dizziness of uncertain cause
- Anxiety
- Hyperventilation
- Labyrinthine disease

RISK FACTORS FOR STROKE

- Definite
  - Modifiable : Cigarette smoking
    Excessive alcohol consumption
    Drug use (cocaine, amphetamines)
  - Non modifiable : Age
    Sex
    Race
    Familial and genetic factors
- Possible
  - Oral contraceptive use
  - Diet
  - Personality type
  - Geographic location
  - Season
  - Climate
  - Socioeconomic factors

        - Physical inactivity
        - Obesity
        - Abnormal blood lipids
    - Disease or disease markers
        - Hypertension
        - Cardiac disease
        - TIA
        - Elevated hematocrit
        - Diabetes mellitus
        - Sickle cell disease
        - Elevated fibrinogen concentration
        - Migraine headaches and migraine equivalents
        - Carotid bruit

HYPERTENSION

- Major risk factor for ischemic stroke
- Present in 50-70% of cases
- There is association between blood pressure and risk of stroke even at a systolic BP of 115mmHg

DIABETES

- Clear risk factor for 1st stroke
- Independent risk factor for recurrent stroke
- Predictor of multiple lacunar infarcts

DYSLIPIDEMIA

- Increased levels of total cholesterol and LDL-C are associated with higher risk of ischemic stroke[39]
- High serum triglyceride is independently associated with ischemic stroke especially large artery atherosclerotic strokes[40]
- Reduced HDL-C is also associated with greater risk of ischemic stroke

SMOKING

- Major independent risk factor for ischemic stroke
- Risk of stroke is also increased in exposure to passive smoking and tobacco smoke in the environment[41].
- Smoking facilitates atherosclerosis
- 5years after smoking cessation, stroke risk of ex-smoker is equal to that of non-smoker

ALCOHOL

- Chronic alcoholism and heavy drinking bear a high risk for all stroke subtypes
- Studies have shown that there is a J shaped association between alcohol and ischemic stroke with the effect that there is protective effect in light or moderate consumption to increased risk in heavy consumption.
- The protective effect is due to raised HDL, decreased platelet aggregation and reduced concentration of plasma fibrinogen
- Increased risk is attributed to alcohol induced hypertension, hypercoagulable state, reduced cerebral

blood flow and atrial fibrillation or cardioembolism due to cardiomyopathy

- Also plays a role in insulin resistance and metabolic syndrome.

OBESITY

- Body Mass Index > 30kg/m^2 is by itself a risk factor for cardiovascular disease
- Major role in primary prevention
- There are no studies to support that weight reduction may reduce the risk of recurrent stroke.

PHYSICAL ACTIVITY

- Exerts beneficial effect on various risk factors for stroke
- Physical activity reduces blood pressure and weight, enhances vasodilatation, improves glucose tolerance and promotes cardiovascular health.

METABOLIC SYNDROME

- Combination of several physiological abnormalities that increase risk of stroke.

- According to American Heart Association criteria, metabolic syndrome is recognized when 3 out of 5 features are present

    I. Increased waist circumference (>102cm in men and >88cm in women)

    II. Increased triglycerides (>150mg/dl)

    III. Decreased HDL-C (<40mg/dl in women and <50mg/dl in men)

    IV. Increased blood pressure (systolic >130mmHg or diastolic >85mmHg)

    V. Increased fasting blood glucose (>100mg/dl)

- Research has redefined the syndrome so as to include subclinical inflammation and disorders of thrombosis, fibrinolysis and endothelial function and theories suggest that it may be transmitted genetically[42].

HEART DISEASE

- The basic pathology being the same, if the coronaries are diseased, arteries to the brain are also likely to be affected.

- Coronary artery disease, congestive heart failure, left ventricular hypertrophy, valvular heart disease and arrhythmias are all associated with greater risk of stroke.

AGE

- Risk of stroke significantly increases with age
- The risk of stroke with advancing age cannot be changed; it has a prime role in assessing stroke risk and planning preventive therapies.

ORAL CONTRACEPTIVE PILLS

- Oestrogen promotes blood clotting
- Low dose oestrogen minimizes the risk

CAROTID BRUIT

- Noise due to turbulent flow in a blood vessel (artery) as a consequence of narrowing due to atherosclerosis.
- Associated with a high risk of ischemic stroke.

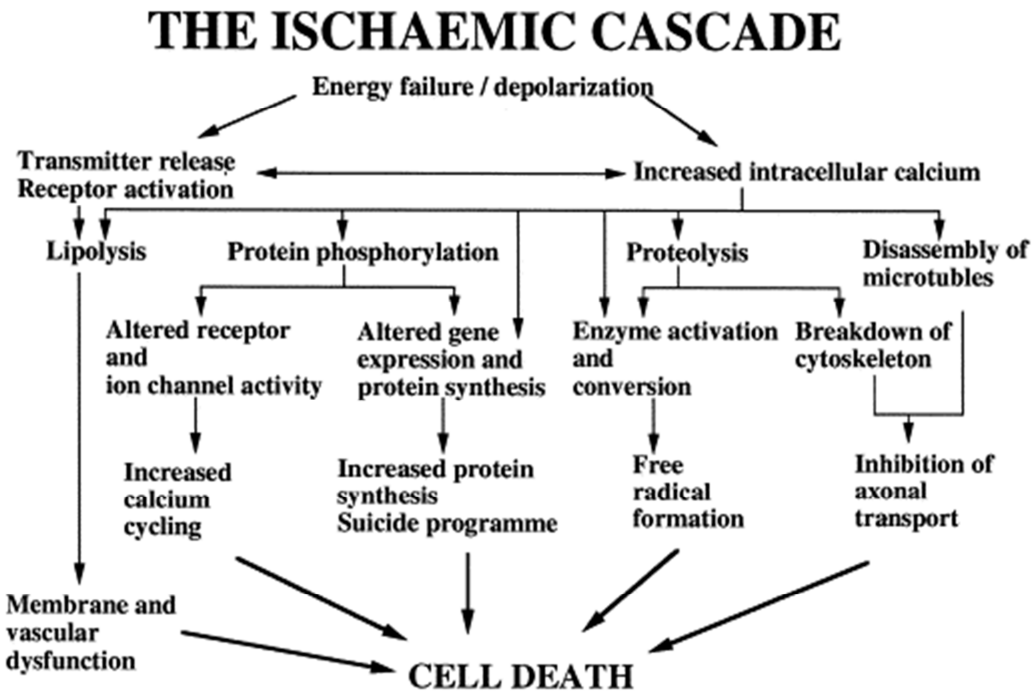


FIGURE NO. 4- ISCHEMIC CASCADE IN THE BRAIN

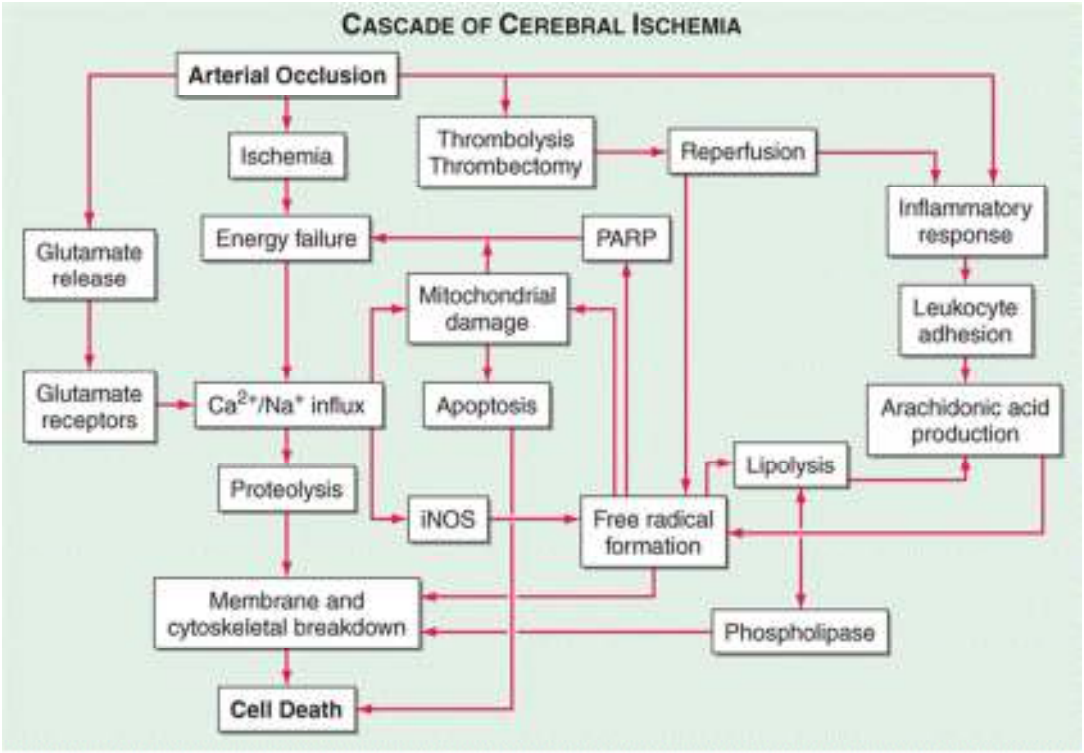


FIGURE NO.5- CASCADE OF CEREBRAL ISCHEMIA

INVESTIGATIONS

- Basic investigations-complete blood count

  Erythrocyte sedimentation rate

  Serum electrolytes

  Blood urea nitrogen

  Serum creatinine

  Blood sugar

  Urine analysis

  Serum lipid profile

- Electrocardiogram
- Chest xray
- Coagulation profile- prothrombin time

  Activated partial thromboplastin time

- Echocardiogram
- Imaging studies
  - CT-scan
    - Imaging modality of choice in acute stroke

- Early identification or exclusion of hemorrhage
- Identification of extraparenchymal haemorrhages, neoplasm, abscess and other conditions mimicking stroke
- Infarct may not be seen reliably for 24-48 hours
- Small ischemic strokes in the posterior fossa are not seen.
- Small infarcts on the cortical surface are missed

- **CONTRAST ENHANCED CT SCAN**
  - Picks up subacute infarcts
  - Allows visualisation of venous structures
  - Highlights the deficits in brain perfusion and shows regions of infracted brain as well as ischemic penumbra
  - Carotid disease and intracranial vascular occlusions are picked up with CT angiography.
- **MRI scan**
  - Reliably detects the extent and location of infarct in all areas of brain including posterior fossa and cortical surface
  - Less sensitive to detect acute bleed

- Diffusion weighted imaging more sensitive for early brain infarction
- MR perfusion studies using Gadolinium contrast pick up ischemic penumbra
- MR angiography detects stenosis of extracranial internal carotid arteries and large intracranial arteries with high sensitivity
- MRI with fat saturation visualises extra or intracranial arterial dissection
- After the acute period, MRI clearly defines the extend of tissue injury and demarcates areas of old infarction from new.
- Highly sensitive to identify areas of new infarction in transient ischemic attack.

- **CONVENTIONAL XRAY CEREBRAL ANGIOGRAPHY**
  - Considered gold standard in identifying and quantifying stenosis of cerebral arteries due to atherosclerosis.
  - CT angiography of entire head and neck may be used in the initial evaluation of stroke.

- Also identifies aneurysms, vasospasm, intraluminal thrombi, arteriovenous fistula, vasculitis, fibromuscular dysplasia and collaterals.

- **Drawbacks**

    - Arterial damage

    - Groin hemorrhage

    - Embolic stroke

    - Contrast nephropathy

- Conventional angiography coupled with endovascular techniques is employed in cerebral revascularisation.

- **ULTRASOUND TECHNIQUES**

    - B mode ultrasound imaging is coupled with Doppler ultrasound for flow assessment(duplex ultrasound)

        - Identifies and quantifies stenosis at origin of internal carotid artery.

    - Transcranial Doppler

        - Assesses flow in middle cerebral artery, anterior cerebral artery, posterior cerebral artery and vertebrobasilar system.

- Combination of MR angiography with these ultrasound studies used in evaluating vascular stenosis

- **PERFUSION TECHNIQUE**

  - Xenon CT and PET

    - Assess and quantify cerebral blood flow
    - Help in the planning of revascularization surgeries

  - Single photon emission computed tomography(SPECT)

    - Measures relative cerebral blood flow

  - CT perfusion imaging

    - When compared with non contrast CT scan, detects ischemia and ischemic penumbra with increased sensitivity

  - MR perfusion imaging

    - Demarcates the ischemic penumbra when combined with MR diffusion imaging

TREATMENT

Immediate Goal : Ensuring perfusion to the ischemic penumbra

Later Goals : Minimising disability

Preventing complications

Preventing recurrence

A. MEDICAL SUPPORT

- Blood pressure
  - Acute blood pressure lowering controversial as collateral blood flow is blood pressure dependent
  - Indications for blood pressure lowering
    - Malignant Hypertension
    - Concomitant myocardial ischemia
    - BP > 185/110mmHg
    - Planning for thrombolytic therapy
- Fever
  - Detrimental
  - Treated with antipyretics and surface cooling

- Serum Glucose
  - Maintained at <180mg/dl
  - Insulin infusion used if necessary
- Cerebral Oedema
  - Peaks on 2nd or 3rd day
  - Causes mass effect for near 10 days
  - More likely with larger infarcts
  - Treated with fluid restriction and IV mannitol which raise serum osmolarity
  - Hypovolemia to be avoided as the resulting hypotension may worsen the infarction
  - Trials have shown that hemicraniectomy markedly reduces mortality
  - Cerebellar Infarction
    - Even small amounts of cerebellar oedema can severely raise the intracranial pressure
    - Cerebellar oedema may directly compress the brainstem causing coma and respiratory arrest

- Emergency surgical decompression may be required
- Prophylactic suboccipital decompression of large cerebellar infarcts is practiced in stroke centres

- Infections
  - Pneumonia, urinary tract infection and bedsores are the common ones encountered
  - Prevented by avoiding aspiration, physiotherapy and prophylactic antibiotics when required
  - Use appropriate antibiotics when needed
- Deep Vein Thrombosis and Pulmonary Embolism

  Prevented using :
  - Pneumatic compression stockings
  - Subcutaneous heparin

B. INTRAVENOUS THROMBOLYSIS

- **INDICATIONS**
  - Clinical diagnosis of ischemic stroke
  - Onset of symptoms to time of drug administration <3hours

- CT scan showing no hemorrhage or oedema of > 1/3rd of the MCA territory
- Age > 18years
- Consent by the patient or surrogate

- **CONTRAINDICATIONS**
  - Sustained BP > 185/110mmHg despite treatment
  - Platelet < 1,00,000
  - Hematocrit < 25%
  - Glucose <50 or >400mg/gl
  - Use of heparin within 48hours and prolonged PTT or elevated INR
  - Rapidly improving symptoms
  - Prior stroke or head injury within 3months
  - Prior intracranial hemorrhage
  - Major surgery in preceding 14days
  - Minor stroke symptoms
  - Gastrointestinal bleeding in preceding 21days

- Recent myocardial infarction
- Coma or stupor

C. ENDOVASCULAR TECHNIQUES

- Intraarterial administration of thrombolytic agent
  - For large clots in the major vessels which fail to open with thrombolysis
  - Not yet approved by US FDA
- Endovascular Mechanical Thrombectomy

  Indications :
  - Ineligible or with contraindications to thrombolytics
  - Failed vascular recanalisation with IV thrombolytics

D. ANTITHROMBOTIC TREATMENT

- Platelet inhibitors
  - Aspirin is the only antiplatelet drug proved to be effective in acute ischemic stroke
  - Use of aspirin within 48hours of stroke onset decreases risk of stroke recurrence and mortality.

- Abciximab, a glycoprotein IIb/IIIa receptor inhibitor, should be avoided in acute stroke as it causes intracranial hemorrhage.

- Anticoagulation

  - The routine use of heparin or other anticoagulation in atherothrombotic stroke is not supported by trials.

E. NEUROPROTECTION

- Measures that attempt to prolong the brain's tolerance to ischemia

  - Hypothermia

  - Drugs that block excitatory amino acid pathway

F. STROKE CENTRES

- A dedicated stroke team improves neurologic outcome and reduces mortality.

- Emergency 24 hour evaluation of patients with acute stroke and considering thrombolysis or endovascular treatments

G. REHABILITATION

- Includes early physiotherapy as well as occupational, and speech therapy.

- educating the patient and family about the patients' neurological deficit and on prevention of complications
- Aims to maximise recovery
- Restraint therapy: immobilizing the affected side improves hemiparesis.

This shows that physical therapy recruits unused neural pathways and the fact suggests that the human nervous system is more adaptable than originally thought.

MODIFIED RANKIN SCALE (MRS)

Patient Name: _____
Rater Name: _____
Date: _____

Score	Description
0	No symptoms at all
1	No significant disability despite symptoms; able to carry out all usual duties and activities
2	Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3	Moderate disability; requiring some help, but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability; bedridden, incontinent and requiring constant nursing care and attention
6	Dead

TOTAL (0–6): _____

SCANDINAVIAN STROKE SCALE

Patient Name: _____
Rater Name: _____
Date: _____

Function	Score	Prognostic Score	Long Term Score
Consciousness:			
-fully conscious	6	___	
-somnolent, can be awaked to full consciousness	4		
-reacts to verbal command, but is not fully conscious	2		
Eye movement:			
-no gaze palsy	4	___	
-gaze palsy present	2		
-conjugate eye deviation	0		
Arm, motor power *:			
-raises arm with normal strength	6	___	___
-raises arm with reduced strength	5		
-raises arm with flexion in elbow	4		
-can move, but not against gravity	2		
-paralysis	0		
Hand, motor power *:			
-normal strength	6		___
-reduced strength in full range	4		
-some movement, fingertips do not reach palm	2		
-paralysis	0		
Leg, motor power *:			
-normal strength	6	___	___
-raises straight leg with reduced strength	5		
-raises leg with flexion of knee	4		
-can move, but not against gravity	2		
-paralysis	0		
Orientation:			
-correct for time, place and person	6		___
-two of these	4		
-one of these	2		
-completely disorientated	0		
Speech:			
-no aphasia	10		___
-limited vocabulary or incoherent speech	6		
-more than yes/no, but not longer sentences	3		
-only yes/no or less	0		
Facial palsy:			
-none/dubious	2		___
-present	0		
Gait:			
-walks 5 m without aids	12		___
-walks with aids	9		
-walks with help of another person	6		
-sits without support	3		
-bedridden/wheelchair	0		
Maximal Score	58		

* Motor power is assessed only on the affected side.

ALBUMIN

- Most abundant plasma protein
- 55-60% of serum protein
- 585 aminoacids which form a single polypeptide chain, with a deficiency of tryptophan and methionine residues and an excess of charged particles.
- Molecular weight: 66500Da
- Xray crystallography reveals tertiary structure of human albumin crystal
- Heart shaped molecule 80x30 Angstrom
- Highly flexible molecules which changes shape readily
- In solution, three domains are arranged in ellipsoid pattern forming low viscosity molecule
- Resilient structure which regains shape easily in physiological conditions due to the presence of disulphide bridges
- Denaturation occurs only in severe nonphysiological changes in temperature, pH and chemical environment

ALBUMIN METABOLISM

Serum albumin concentration depends on the rate of its production and degradation and also its distribution in the intravascular as well as the extravascular compartments. The total body albumin pool is about 3.5-5kg body weight. 42% of this is in the plasma and the rest is in the extravascular compartment. A part of this is tissue bound and hence out of circulation. There is a daily loss of 120-145g of albumin into the extravascular space, most of which is carried back into the circulation by lymphatic drainage. There is an intestinal loss of about 1g/day and after digestion, there is reabsorption of amino acids and peptides. About 70kg of albumin passes through the kidneys everyday, of which a few grams are filtered through the glomerulus. This is almost completely reabsorbed and finally only 10-20mg of albumin is lost through urine everyday.

EXTRAVASCULAR POOL OF ALBUMIN

- Skin, though compromises only 18% of body weight, has 41% of total extravascular albumin.
- Muscle, which forms 45.5% of body weight, contains 40% of extravascular albumin.
- Gut and liver, which constitute 2.8% and 4.1% body weight respectively, have 7% and 3% of extravascular albumin respectively.

- Subcutaneous tissue, which forms 8% of body weight, contains 9% of albumin.
- Extravascular pool has exchangeable and remote components
- Albumin escapes into extravascular compartment across capillaries
- Half of this occurs through continuous capillaries facilitated by an active transport mechanism
- Rate of escape from the circulation depends on the permeability of the vessel wall and the hydrostatic and oncotic pressures on both sides of the wall (Starling's law)
- Albumin binds to the surface receptor- ALBONDIN
- Albondin is present in most of the capillary beds except in the brain
- Bound albumin enters the vesicles on the endothelial cell and gets released on the interstitial side .
- Rate of transfer increases on the addition of long chain fatty acids, with cationisation and with glycosylation[43].

SYNTHESIS

- Synthesised only by liver in humans
- Liver can increase the synthesis to 2-2.7 times the normal
- Secreted into the portal circulation soon after manufacture

- In healthy young adult, rate of synthesis is 194mg/kg/day, about 12-25gm/day
- Albumin synthesis requires a suitable nutritional, hormonal and osmotic environment
- Colloid osmotic pressure of the interstitial fluid surrounding the hepatocyte regulates albumin synthesis
- Requirements for synthesis
    - mRNA for translation
    - adequate supply of amino acids, activated by binding to tRNA
    - ribosomal machinery for assembly
    - energy as ATP or/and GTP

Factors causing reduced albumin synthesis(table No 1)

Decreased gene transcription	o trauma, sepsis o hepatic disease o diabetes o decreased growth hormone o decreased steroids
Ribosomal disaggregation	Decreased nutritional intake

A decrease in gene transcription causes decreased mRNA concentration. This occurs in acute phase reactions where it is mediated by cytokines mainly interleukin-6 and tumour necrosis factor alpha, rate of albumin synthesis is controlled by the mRNA concentrations available for action on ribosomes. mRNA content is decreased in trauma and diseases processes. Decreased gene transcription is also seen in hepatoma cells and in hepatocytes damaged by carbon tetrachloride

Albumin synthesis requires insulin . Decreased synthesis in diabetes improves the insulin supplementation. Growth hormone stimulates gene transcription in hepatocytes[44].

Steroids have a complex role on albumin synthesis. Combination of steroids with insulin or aminoacids causes increased synthesis. But steroids also cause increased albumin catabolism.

Fasting reduces albumin production and protein restriction decreases it all the more. In the early phase of protein deprivation, the disintegration of free and bound polysomes can be reversed by refeeding with aminoacids -equally tryptophan with ornithine. Tryptophan is incorporated into albumin, but ornithine is not. Prolonged protein deprivation causes a 50-60% decrease in the concentration as well as activity of mRNA. Energy is more important than aminoacids under normal circumstances for polysome aggregation. Reduced synthesis in starvation is found to correct with glucose refeeding alone which causes polysome reaggregation.

DEGRADATION

- total daily albumin degradation is 0.2g/kg/day
- this constitutes 5% of daily whole body protein turnover

Most of the organs of the body are involved in the breakdown f albumin. 40-60% of albumin is broken down by muscles and skin. 10% leaks into gastrointestinal tract via stomach wall. Kidneys are responsible for another 10%. Though the liver has a high rate of metabolism, it degrades less than 15%.

Endothelial surface membrane scavenger receptors,gp18 and gp30 bind to altered , denatured albumin. This is taken up by the endocytic vesicles which fuse with the lysosomes in the endothelial cells. Cell modification of the circulating albumin is a signal for receptor-linked lysosomal degradation.

Chemical modification may also prevent degradation. it is protected from breakdown by the binding of long chain fatty acids to albumin, in hypoalbuinemia, the ratio of long chain fatty acids to albumin increases and breakdown is suppressed.

The final products of degradation are amino acids. These join the amino acid pool inside the cells and in the plasma.

FUNCTIONS OF ALBUMIN

A. MAINTAINING ONCOTIC PRESSURE

Albumin has higher concentration in plasma than other plasma proteins, it has a molecular weight of 66.5kDa. Though this is less than the average weight of globulin(147kDa), albumin has great osmotic impact. Because of the higher molecular weight and plasma concentrations, in health, albumin contributes 80% of the normal oncotic pressure.60% of this is due to the direct osmotic effect. Negative charges of the molecule is responsible for the remaining 40%, this negative charge is responsible for the attractive force that leads to intravascular retention of positively charged solute particles(Gibbs-Donnan effect).

Albumin, because of its large extra vascular pool, solubility in water and net negative charge, has a major role in the regulation of tissue fluid distribution.

B. BINDING OF SUSTANCES

Albumin has a structure that can incorporate several different substances. Also the structure is flexible and bound substances can be buried within its structure. The charge of the binding substances and the strength of binding have no correlation.

- Substances that bind most strongly to albumin: medium-sized hydrophobic organic anions – long chain fatty acids, bilirubin, hematin
- Substances that bind specifically but with less affinity : Ascorbate, tryptophan
- Chirality of the substance also determine the strength of binding
- Divalent cations like calcium and magnesium bind, but monovalent cations do not
- Basic drugs tend to bind to albumin
- Endogenous substances that bind to albumin: eicosanoids, copper, zinc, folate, aquacobalamin, bile acids
- Secondary or tertiary carrier for substances with specific binding protein:

Steroids, vitamin D, Thyroxine

Drug Binding

Binding of the drug to albumin affects its delivery to tissue and also its metabolism and eliminations. This also determines the free serum concentration of the drug. Highly bound drugs have less concentration of their free form in serum. Drug-albumin interactions are responsible for the wide inter-individual variations in response to drugs. Factors like age, temperature,

Ph and ionic strength influences the drug-albumin interactions. These alter the number of functional binding site and thereby the distribution, pharmacological action, metabolism and excretion of the displaced drug are altered.

Binding sites on albumin are broadly classified into site I and site II.

Site I: along the long loop of subdomain IIa, extending into the shorter loop.

Drugs binding to this site: salicylates, werfarin, phenylbutazone, indomethacin, digitoxin, furosemide, phenytoin, chlorpropamide, pencillins, dyes like sulfobromophthalein, iophenoxate, Methyl red, Evans blue, bromocresol green, Biliurubin

Site II : hydrophobic pocket of residues in subdomain IIIa

Substances binding to this site: L-Tryptophan,thyroxine, chloride, medium-chain fatty acids, diazepam, bendodiazepine, ibuprofen, naproxen, clofibrate

C. METABOLIC FUNCTIONS

Albumin causes the inactivation of certain compounds like disulfiram, penem group of antibiotics etc. Because of the avidity of binding, albumin has a role in the metabolism of substances like lipids and eicosanoids. Albumin stabilises eicosanoids like prostaglandin I_2 and thromboxane A_2. It also releases arachidonic acid from macrophages and favours lipoxygenases activity over that of cycloxygenase.

Penicillin allergy is due to irreversible coupling of penicilloyl groups to lysine group in site 1. This causes production of antibodies to drug-albumin complex.

D. ACID-BASE FUNCTION

Albumin acts as an effective buffer by its relative abundance in plasma as well as the presence of charged residues on the molecules. At physiological pH, albumin contributes to half the normal anion gap with a net negative charge of 19. A decrease in serum albumin of 1g/dl increases the standard bicarbonate by 3.4mmol/L , thereby causing a reduction in the anion gap by 3mmol/L.

E. ANTIOXIDANT FUNCTION

Albumin has antioxidant properties under physiological conditions. It scavenges the free radicals which are involved in the pathogenesis of various diseases. The production of oxygen free-radicals by activated polymorphonuclear leucocytes from the enzyme myeloperoxidase is also inhibited by physiological solutions of human albumin. This action is due to the sulfhydrl groups on albumin.

F. MAINTAINING MICROVASCULAR INTEGRITY

Albumin controls the stress-induced increase in capillary permeability. This action is brought about by the endothelial cells which alter the permeability of the capillary membrane by tweaking the nature and distributions of glycoprotein in the vessel wall. This may be due to the negative

charge of the molecule or the reduction in the size of channels by the albumin molecule. Albumin prevents the apoptosis of endothelial cells, the peak action being at physiological concentrations.

Albumin slows the onset and enhances the vasodilatory response to nitric oxide. Nitric oxide by binding to the sulfhydryl groups of albumin, forms the S-nitrosothiol group which is not rapidly degraded. Thus albumin plays a role in the regulation of vasodilatory tone of vessels.

G. ANTICOAGULANT EFFECTS

Has a heparin-like action due to resemblance in the structure of molecules with plenty of negatively charged groups. Heparin exerts its anticoagulant effect by negatively charged sulphate groups to the positively charged groups on antithrombin III. Albumin enhances the neutralisation of factor Xa by anithrombin III. This explains the negative correlation between albumin concentration and heparin requirements in patients on hemodialysis. This might also explain the hypercoagulable state occurring in nephrotic syndrome. Albumin also exerts an inhibitory effect on platelet aggregation both dependant and independent of the cycloxygenase system.

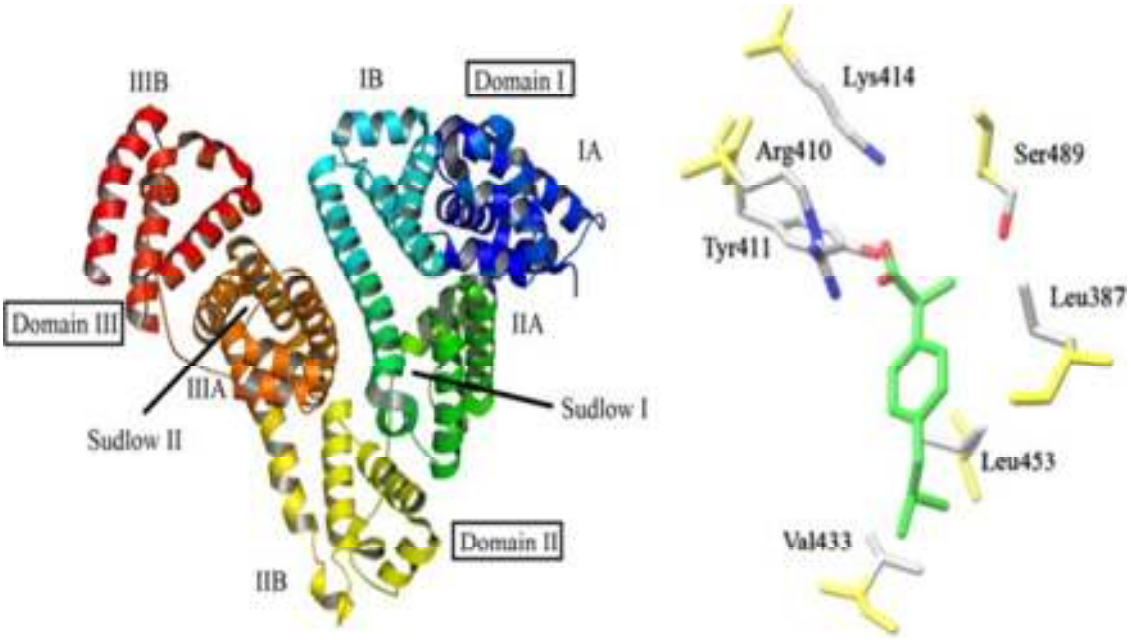


FIGURE NO.6- STUCTURE AND BINDING SITES ON ALBUMIN MOLECULE

ANALBUMINEMIA

Albumin has large number of variants , about 100, based on the electrophoretic mobility. Only one variant, which has high affinity for thyroxine, is known to affect the function of albumin, thereby causing Familial Dysalbuminemic Hyperthyroidism[46].

Analbuminemia has also being defined as serum albumin concentration of less than 1g/litre. There is a small amount of albumin in circulation which is adequate under normal conditions. But in times of stress, when the requirements shoot up, features manifest. It is a rare condition which may be

sporadic or familial . if familial, it has autosomal recessive inheritance. Albumin gene is present, but genetic mutations produce effects which prevent translation.

Cases usually present in adulthood. The features are:

- Peripheral oedema
- Lipodystrophy causing lower limb obesity
- Fatigue
- Hyperlipidemia without atherosclerosis
- Reduced osmotic pressure
- Decrease in arterial pressure causing increased rennin and aldosterone concentrations.

Body tries to compensate for the low serum albumin by slowing the rate of degradation.

ALBUMIN IN CRITICAL ILLNESS

Critical illness brings about changes in the distribution and metabolism of albumin.

CHANGES IN DISTRIBUTION

There is alteration in the distribution of albumin between the intravascular compartment and the extravascular compartment. The underlying

pathology is an increased capillary leakage. There occurs endothelial dysfunction, causing capillary leakage and loss of proteins, inflammatory cells and large volumes of fluid into the interstitial space. The mediators of this process are:

- Endotoxins of gram-negative bacteria
- Cytokines-TNF-alpha and IL-6
- Leukotriene and prostaglandins
- Complement components –C3a and C5a
- Vasoactive peptides like bardykinin and histamine
- Chemokine like macrophage inflammatory protein 1alpha

This altered distribution is predominantly seen in sepsis and after major surgical stress. The trans-capillary escape rate increases upto 300% in septic shock and by 100% after cardiac surgery. In sepsis, this improves with appropriate treatment. When albumin moves out of the vascular compartment, there is a resultant increase in lymphatic flow intravascularly. There is a 30% reduction in the total circulating and total exchangeable albumin pools following major surgery. This is mainly due to sequestration of albumin in non-exchangeable sites , for example-wounds, intestine and extra-abdominal sites.

CHANGES IN METABOLISM

There occurs alteration in the synthesis and degradation of albumin resulting in a dramatic decrease in serum albumin concentrations even early in the course of a critical illness[47].

Synthesis

In trauma, inflammation or sepsis, the acute phase response involves an increase in the gene transcription rate of positive acute phase proteins like C-reactive protein and a decreased rate of albumin synthesis. The decreased synthesis is due to reduced gene transcription which is mediated by IL-6 and TNFalpha. A sustained inflammatory response results in prolonged inhibitions of albumin synthesis.

Catabolism

The degradation rate is mass dependent. So when serum albumin concentration decreases, degradation rate also decreases. But in increased transcapillary escape of albumin, there is an increase in degradation rate. Vascular endothelium is thought to play a major role in the degradation of albumin. More of tissue exposure in the presence of increased capillary permeability may increase catabolism. But in myxoedema, though there is an expansion in the extravascular pool of albumin, there is decreased degradation which could be due to the tissue exposure and trapping which protects the albumin from degradation.

There is a huge difference in the kinetics of intravenous albumin between critically ill and healthy subjects. The point of interest in this aspect is that increasing the intravascular albumin concentration using exogenous albumin may be beneficial in critical illness.

Oncotic pressure is low in patients who are critically ill and this may be associated with increased mortality and morbidity. There are arguments that supplementation of albumin can increase the oncotic pressure and thereby avoid life threatening complications like pulmonary oedema. At the same time, there are studies which suggest that pulmonary dysfunction in sepsis is independant of oncotic pressure.

Drug-albumin interactions are altered in critical illnesses. In renal failure, there is accelerated loss of albumin through damaged glomeruli. The binding of drugs to albumin is also altered in renal failure, probably by alteration in the pH and the accumulation of substances which compete with drugs for the binding sites. This results in increased free fraction of drugs causing enhanced drug effect in renal failure. Thus it becomes necessary that the free serum levels of drugs should be monitored in renal failure in order to avoid toxicity.

PROGNOSTIC VALUE OF SERUM ALBUMIN

Serum albumin acts as an independent predictor of mortality in various clinical settings. Serum levels of albumin may also serve as a marker of subclinical disease in elderly patients. Studies in hospitalised patients have revealed that low serum concentration of albumin is associated with prolonged hospital stay, more complications and higher mortality. It also correlates with the prolongation of stay in intensive care unit, increased ventilator requirements and escalating rate of infections. The daily trend of serum albumin may be used as a guide to predict the weaning capability of patients on mechanical ventilation[48]. Serum albumin values at 24-48hours of ICU admission were found to be as good as APACHE II score in predicting mortality. APACHE III system takes serum albumin value into consideration and has better predictive value for mortality in critical illness[49]. Serum albumin, though considered a measure of nutrition, is not a reliable marker of the nutritional status in those who are critically ill.

INTRAVENOUS ALBUMIN THERAPY

There is no proven benefit for intravenous albumin over other colloids in volume replacement in critically ill patients.

Serum albumin has a beneficial role in burns patients. In the first 24 hours, there is a gross increase in capillary permeability with marked transcapillary fluid shifts. Beyond 24 hours, intravenous albumin promotes reabsorption of plasma. According to the Guidelines Of The Consensus

conference in Paris[50], burns less than 15% of body surface area do not require albumin. Those involving more than 50% of body surface area require albumin right from the start of treatment. For those in between, albumin supplementation can wait 24 hours.

Albumin therapy is also beneficial in cirrhotic patients with ascites who require paracentesis. Post-paracentesis circulatory dysfunction which is the increased plasma rennin activity 6 days after paracentesis is prevented by albumin therapy.

LIMITATIONS

- Injudicious use can cause fluid overload due to plasma expansion.
- Myocardial depression probably due to binding of calcium ions.
- Allergic reactions- mostly to contaminants in solution or polymers formed during storage
- Viral transmission though unlikely due to prolonged heat treatments during preparation[51], there is theoretical risk of Creutzfield- Jakob disease.
- Expensive

More of research and interventional studies are required and several controversies to be cleared before albumin therapy becomes an accepted treatment modality to reduce mortality in critically ill patients.

MATERIALS AND METHODS

This observational study was conducted in Coimbatore medical college over a period of one year from july 2017 to june 2018. Approval was obtained from the Ethics Committee, Coimbatore medical college.

The study population consisted of 100 patients who got admitted in medical wards of our hospital with first instance of ischemic stroke within the first 72 hours of onset of symptoms. These patients were included in the study after getting informed consent either from the patient or from the legal guardian.

Study design- longitudinal study

Exclusion criteria:

- Acute haemorrhagic stroke, ischemic stroke with hemorrhagic transformation or stroke related to intracranial space occupying lesion (ICSOL).
- Past history of stroke
- Patients presenting more than 72 hr after the onset of stroke
- Patients with diagnosed malignancy
- Patients with history of chronic liver disease, chronic heart failure, chronic kidney disease or dementia
- Patients with fever or infections

Inclusion criteria

- Patients admitted in medical wards with clinical diagnosis of first onset acute ischemic stroke
- Clinical diagnosis confirmed by CT scan
- Informed consent to participate in the study

Cases where defined as per WHO definition of stroke. Hypertension was documented if there were records proving it or when at least 2 readings of blood pressure - systolic blood pressure was ≥140 mm Hg and diastolic blood pressure was ≥90 mmHg after the acute phase of stroke. Coronary artery disease was diagnosed with either ECG changes or previous records. Patient was considered a smoker if he had a history of smoking in the past 5 years.

About 243 consecutive patients who were admitted in the medical wards with first ever attack of stroke were screened to get the study population of 100. A detailed history was elicited from the attenders, followed by general examination, an elaborate CNS examination and relevant examination of other systems. Vitals were stabilised, and patients underwent a CT scan of the brain- in order to rule out hemorrhagic stroke or any mass lesion. Severity of stroke was graded using the Scandinavian Stroke Scale(SSS). Basic investigations like complete hemogram-including ESR, blood sugar, renal function test, liver function test and serum proteins-albumin and globulin, lipid profile and urine routine examination.ECG was taken to establish any coronary artery disease.

Those that fell under exclusion criteria were excluded. Treatment was initiated and carried out according to the institution guidelines.

Serum albumin was measured using Bromocresol Green.

Patients were followed up, and after 90 days following the onset of stroke, were evaluated either in person or over the phone using the Modified Ranking scale to assess their functional status.

The collected data was entered into Microsoft Excel spreadsheet and analysed statistically .The significance of association was tested using Anova and Kruskal wallis test. Statistical analysis was carried out to establish whether a statistically significant association exist between serum albumin level on admission and the stroke severity, as well as the functional outcome at the end of 90 days. The secondary outcomes that were aimed to be tested included the association with risk factors and the viability of the stroke scales.

RESULTS

TABLE NO 2: DISABILITY BASED ON MRS SCORE

DISABILITY (MRS SCORE)	NO OF PATIENTS	PERCENTAGE
MILD	23	23%
MODERATE	23	23%
SEVERE	29	29%
DEATH	25	25%

CHART NO 1

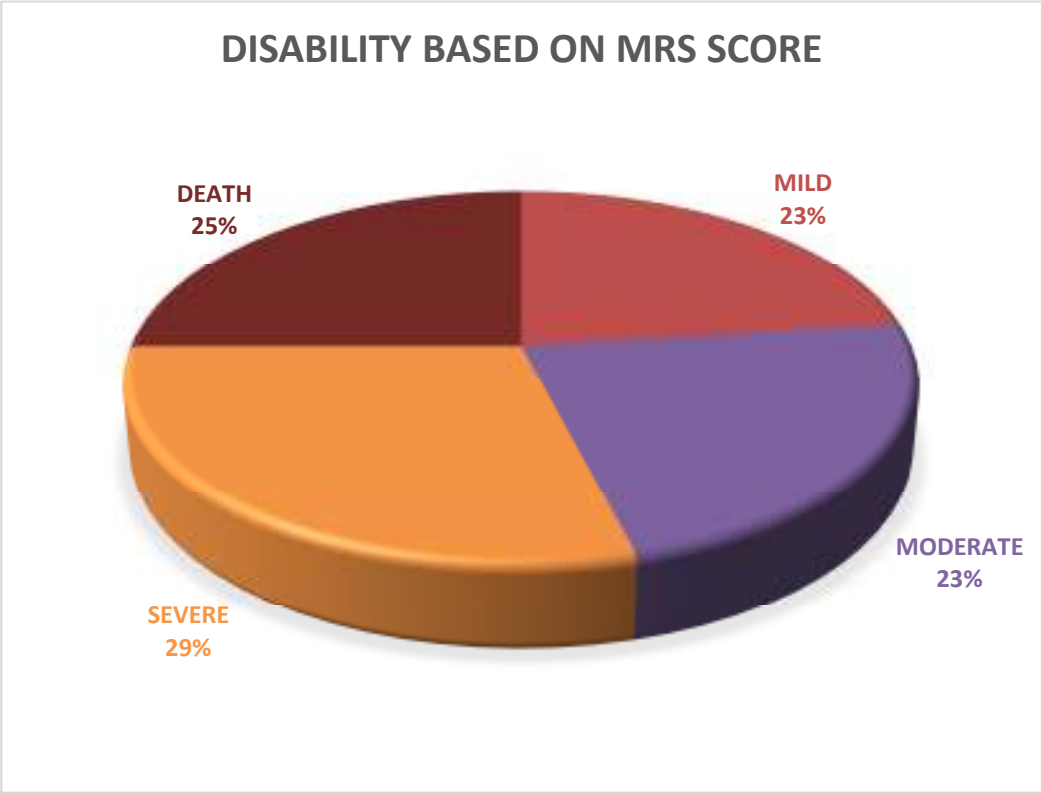


TABLE NO 3:AGE DISTRIBUTION

AGE IN YEARS	NO OF PATIENTS	PERCENTAGE
< 40	13	13%
41-50	22	22%
51-60	24	24%
61-70	20	20%
> 70	21	21%

CHART NO 3

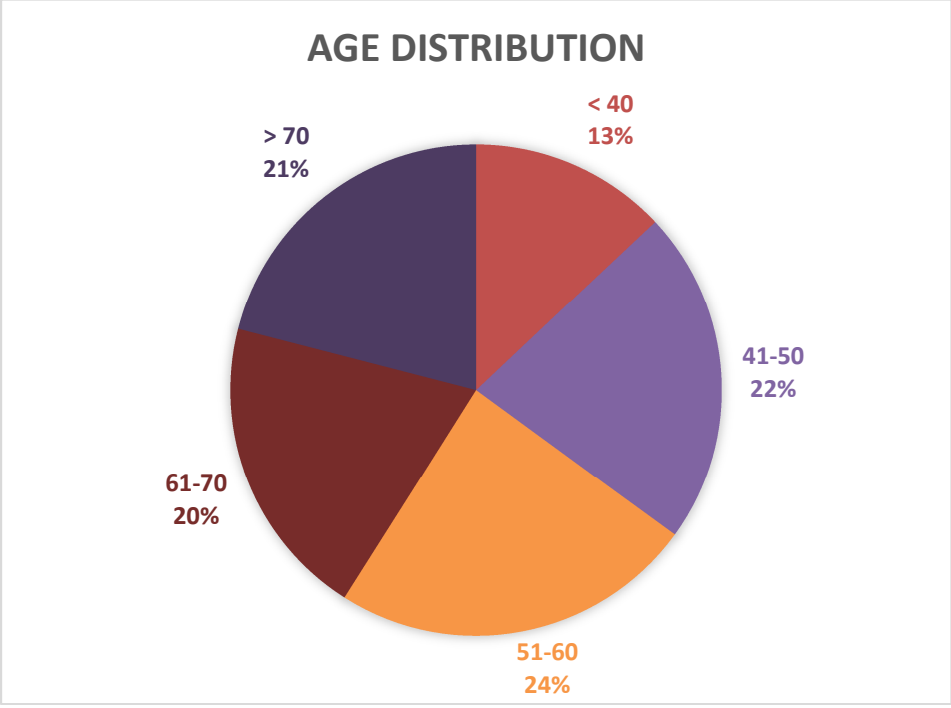


TABLE NO 4: AGE VS DISABILITY

DISABILITY (MRS SCORE)	AGE IN YEARS	
	MEAN	SD
MILD	61.87	13.48
MODERATE	52.39	13.8
SEVERE	58.9	15.34
DEATH	57.24	13.2
ANOVA		
P VALUE - 0.144		
NON SIGNIFICANT		

CHART NO 3

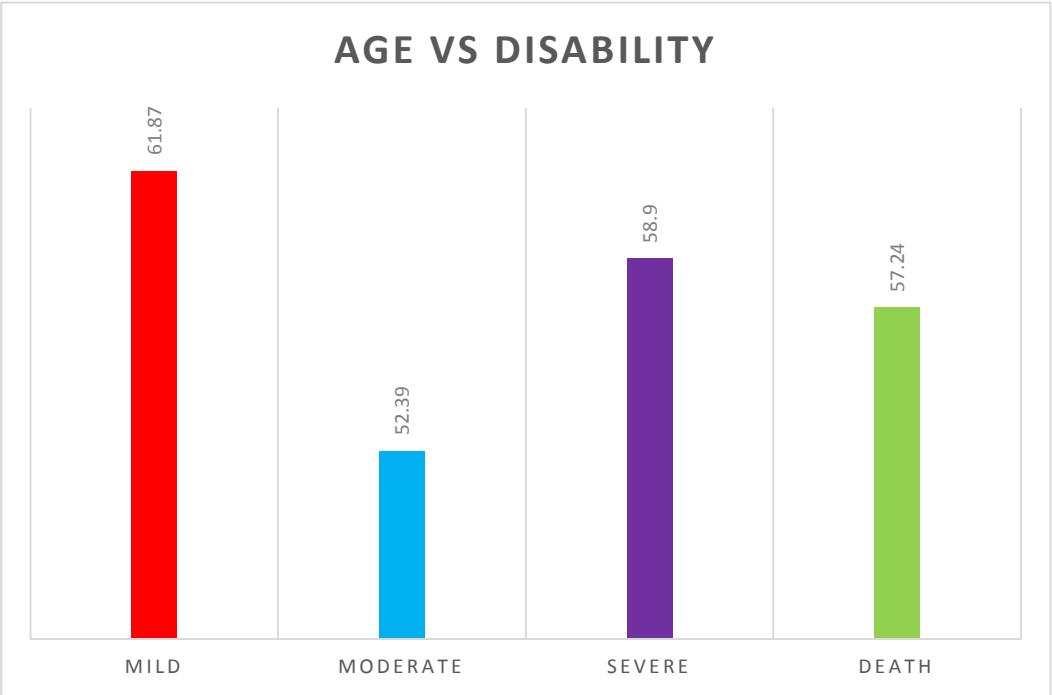


TABLE NO 5:SEX DISTRIBUTION

SEX	NO OF PATIENTS	PERCENTAGE
MALE	54	54%
FEMALE	46	46%

CHART NO 4

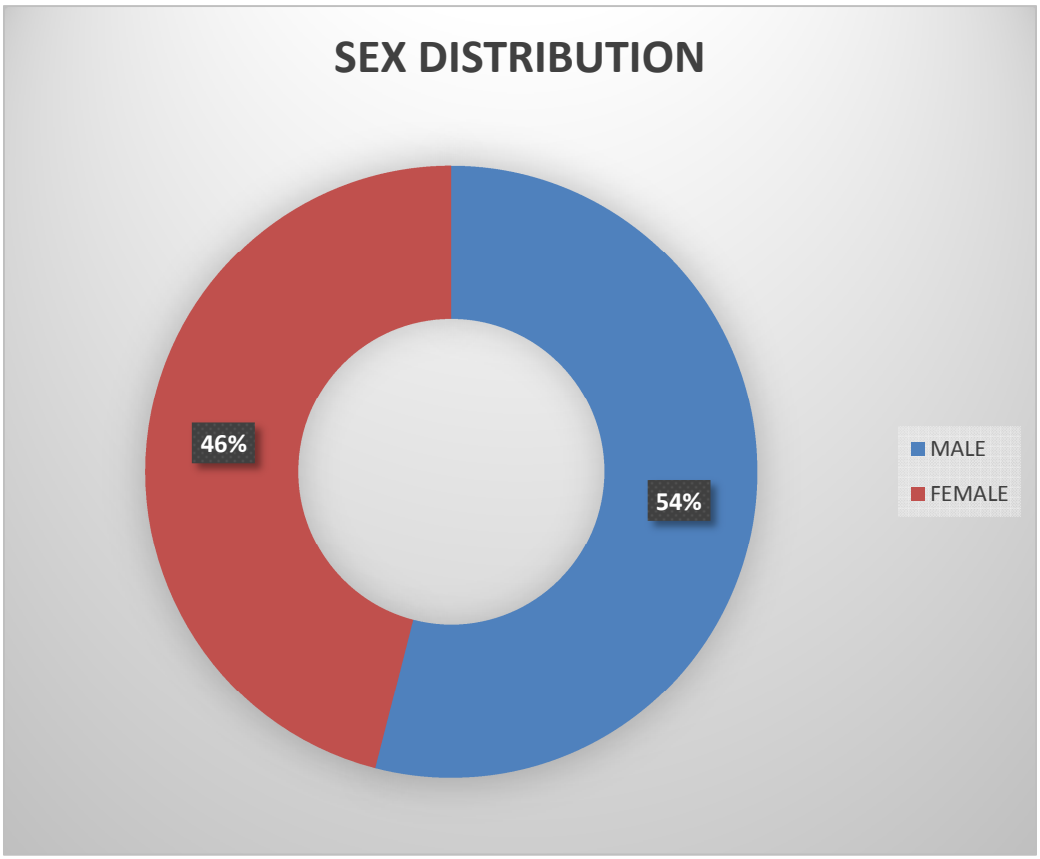


TABLE NO 6: SEX VS DISABILITY

DISABILITY (MRS SCORE)	SEX	
	MALE	FEMALE
MILD	14	9
MODERATE	12	11
SEVERE	15	14
DEATH	13	12
KRUSKAL WALLIS TEST		
P VALUE - 0.904		
NON SIGNIFICANT		

CHART NO 5

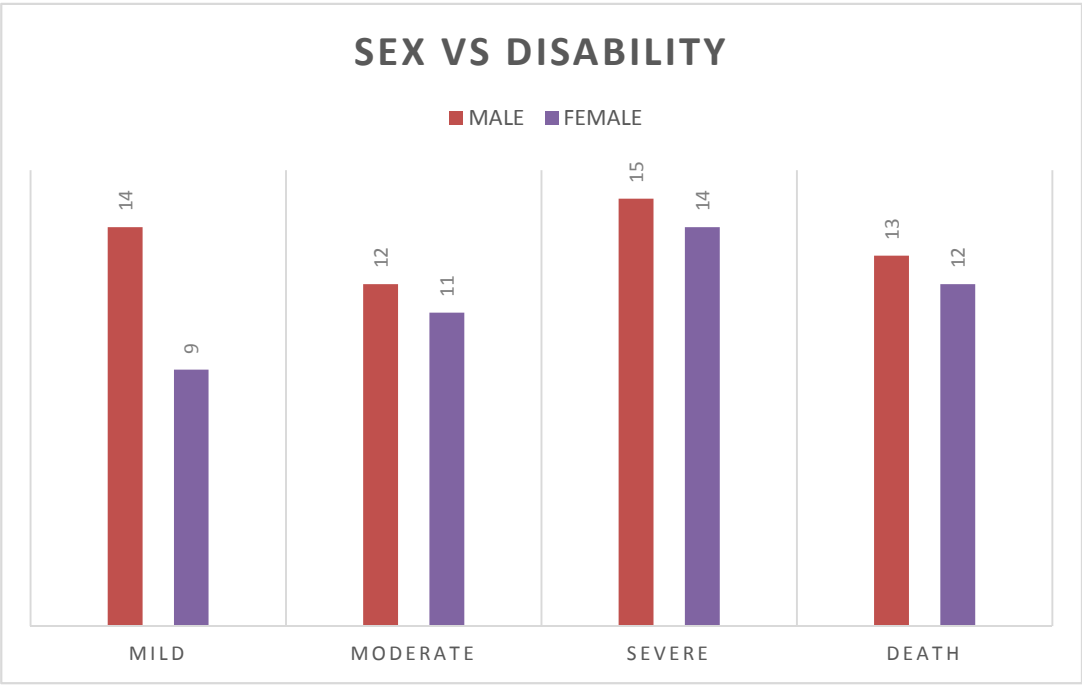


TABLE NO 7:PREVALENCE OF SYSTEMIC HYPERTENSION

SYSTEMIC HYPERTENSION	NO OF PATIENTS	PERCENTAGE
PRESENT	57	57%
ABSENT	43	43%

CHART NO 6

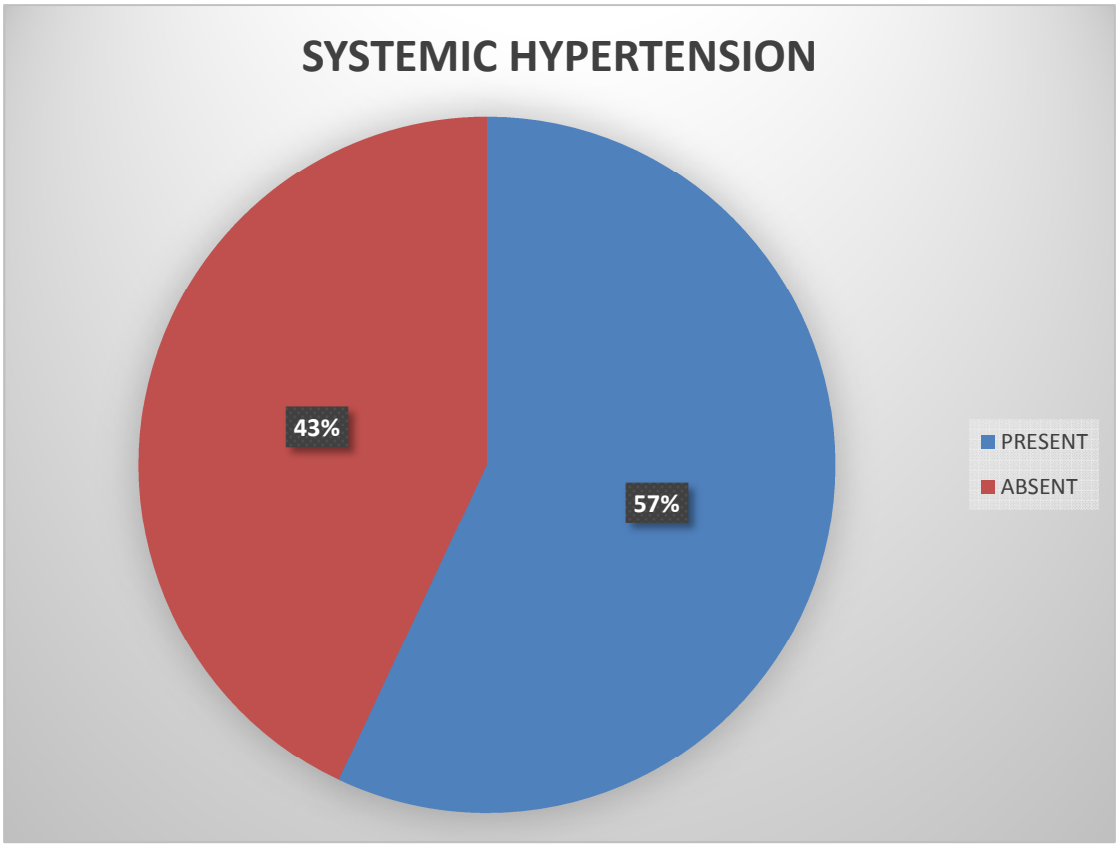


TABLE NO 8: SYSTEMIC HYPERTENSION VS DISABILITY

DISABILITY (MRS SCORE)	SYSTEMIC HYPERTENSION	
	PRESENT	ABSENT
MILD	12	11
MODERATE	14	9
SEVERE	18	11
DEATH	13	12
KRUSKAL WALLIS TEST		
P VALUE - 0.821		
NON SIGNIFICANT		

CHART NO 7

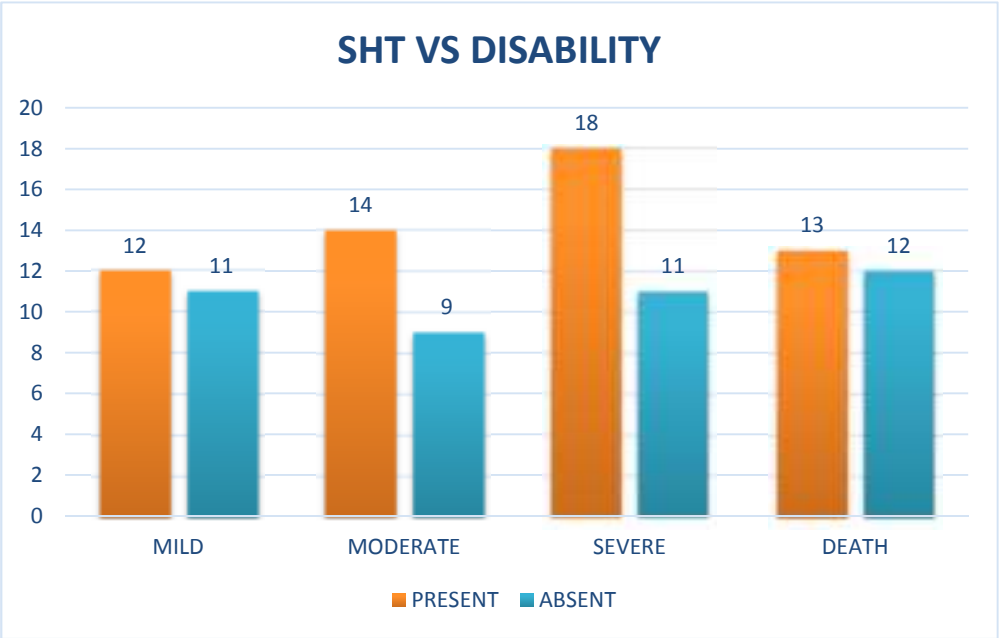


TABLE NO 9: PREVALENCE OF TYPE 2 DIABETES MELLITUS

TYPE 2 DM	NO OF PATIENTS	PERCENTAGE
PRESENT	27	27%
ABSENT	73	73%

CHART NO 8

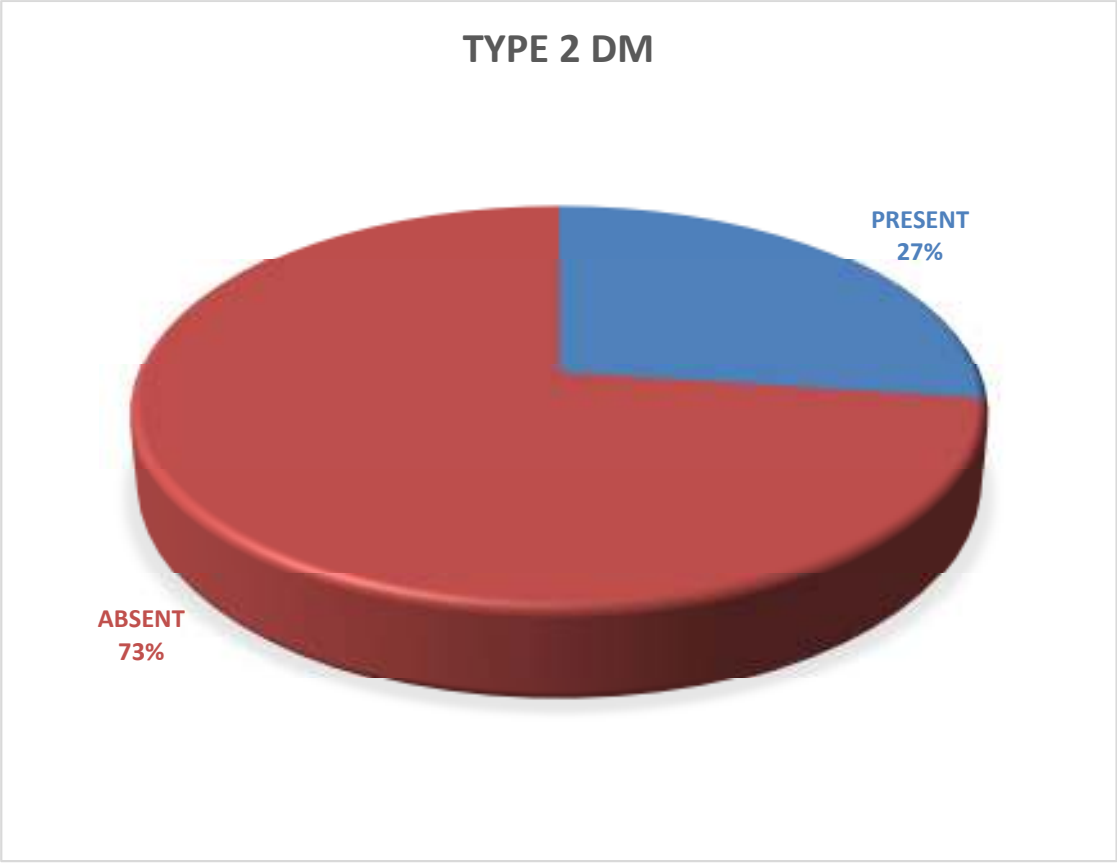


TABLE NO 10: TYPE 2 DIABETES MELLITUS VS DISABILITY

DISABILITY (MRS SCORE)	TYPE 2 DM	
	PRESENT	ABSENT
MILD	8	15
MODERATE	8	15
SEVERE	5	24
DEATH	6	19
KRUSKAL WALLIS TEST		
P VALUE - 0.403		
NON SIGNIFICANT		

CHART NO 9

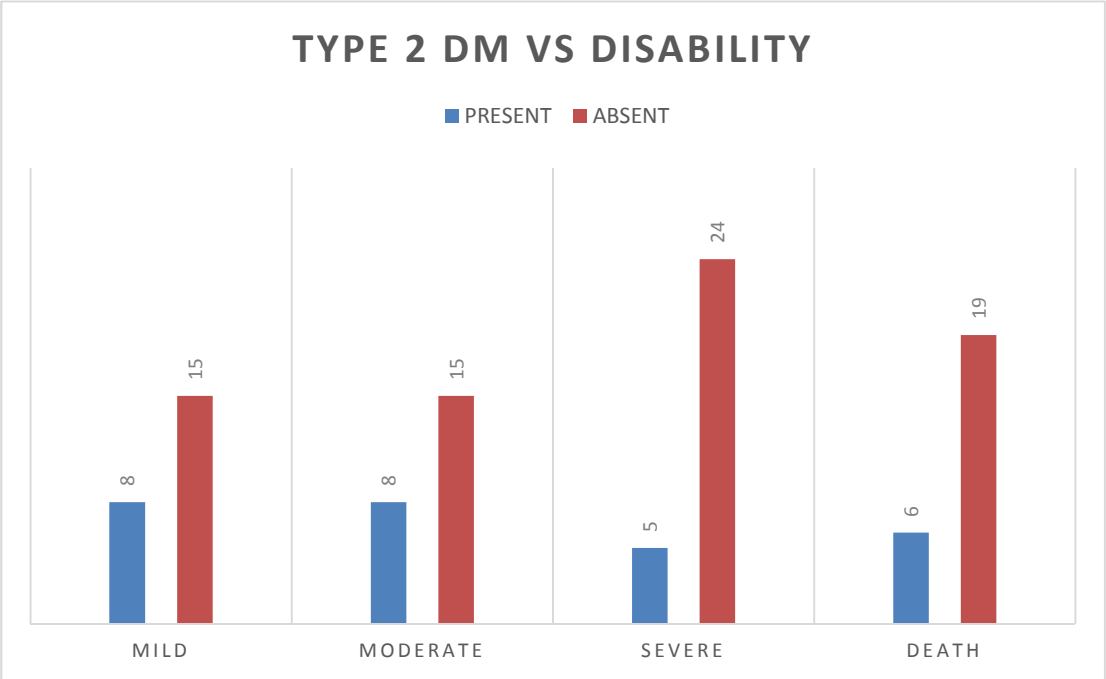


TABLE NO 11: PREVALENCE OF OTHER CO MORBIDITIES

OTHER DISEASES (N=18)	NO OF PATIENTS	PERCENTAGE
CAD	8	44%
DYSLIPIDEMIA	11	61%
RHD	2	11%

CHART NO 10

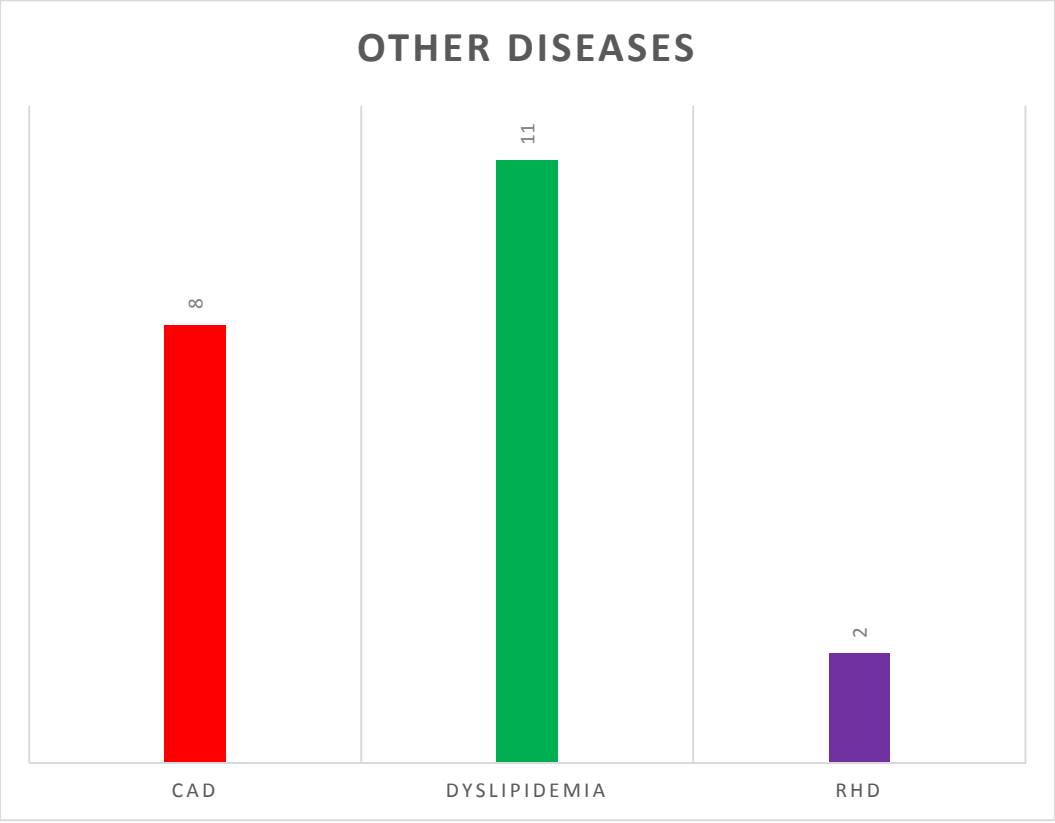


TABLE 12: DISABILITY VS OTHER COMORBIDITIES

DISABILITY (MRS SCORE)	OTHER DISEASES	
	PRESENT	ABSENT
MILD	3	20
MODERATE	3	20
SEVERE	9	20
DEATH	3	22
KRUSKAL WALLIS TEST		
P VALUE - 0.194		
NON SIGNIFICANT		

CHART 11

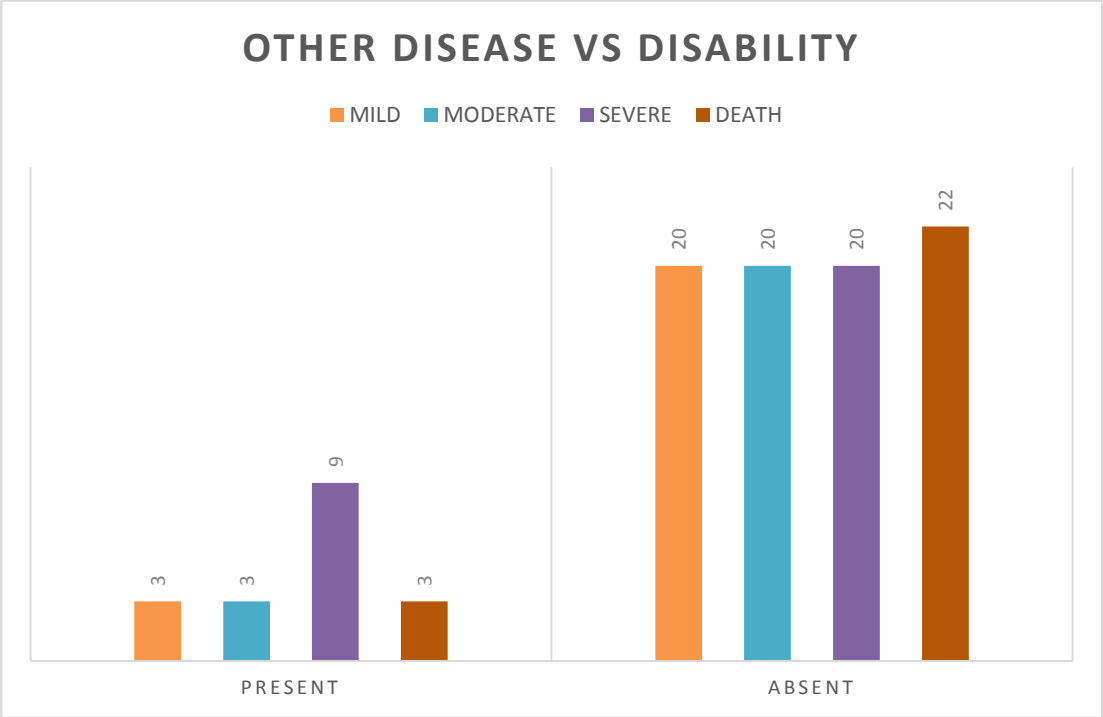


TABLE 13: PREVALENCE OF ADDICTIVE HABITS

ADDICTION (N=32)	NO OF PATIENTS	PERCENTAGE
SMOKING	26	81%
ALCOHOL	9	28%

CHART NO 12

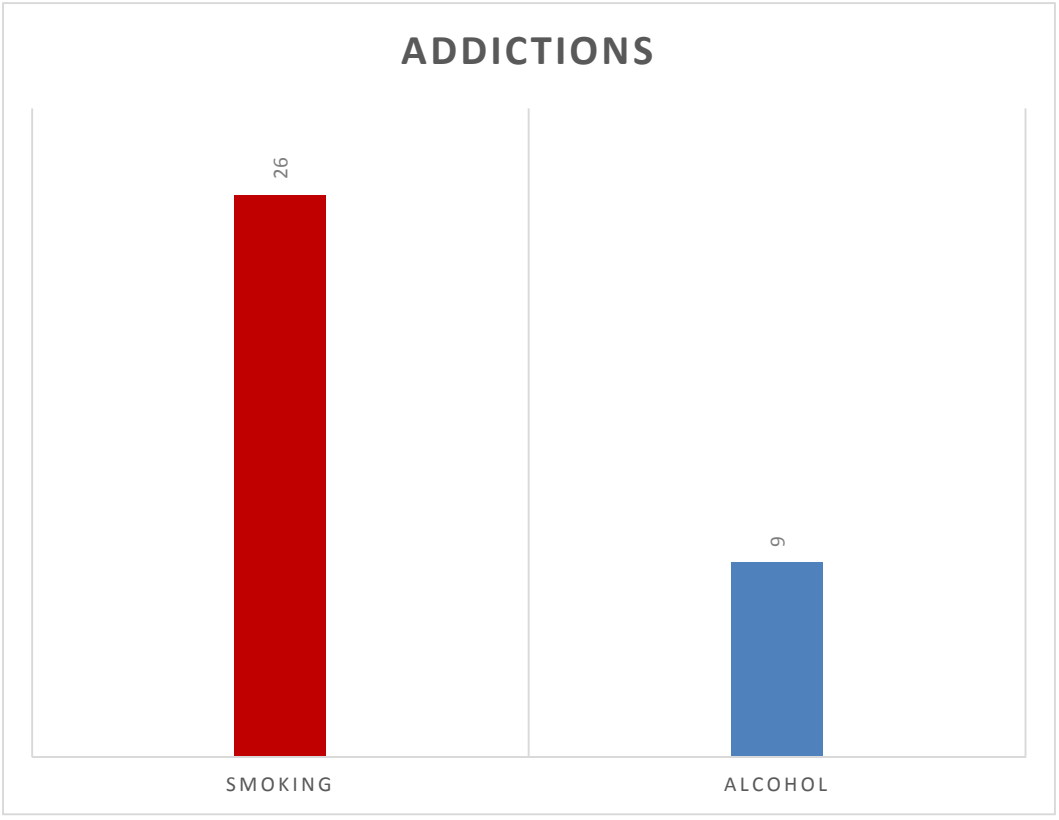


TABLE NO 14: DISABILITY VS ADDICTION

DISABILITY (MRS SCORE)	ADDICTION	
	PRESENT	ABSENT
MILD	9	14
MODERATE	7	16
SEVERE	8	21
DEATH	8	17
KRUSKAL WALLIS TEST		
P VALUE - 0.844		
NON SIGNIFICANT		

CHART NO 13

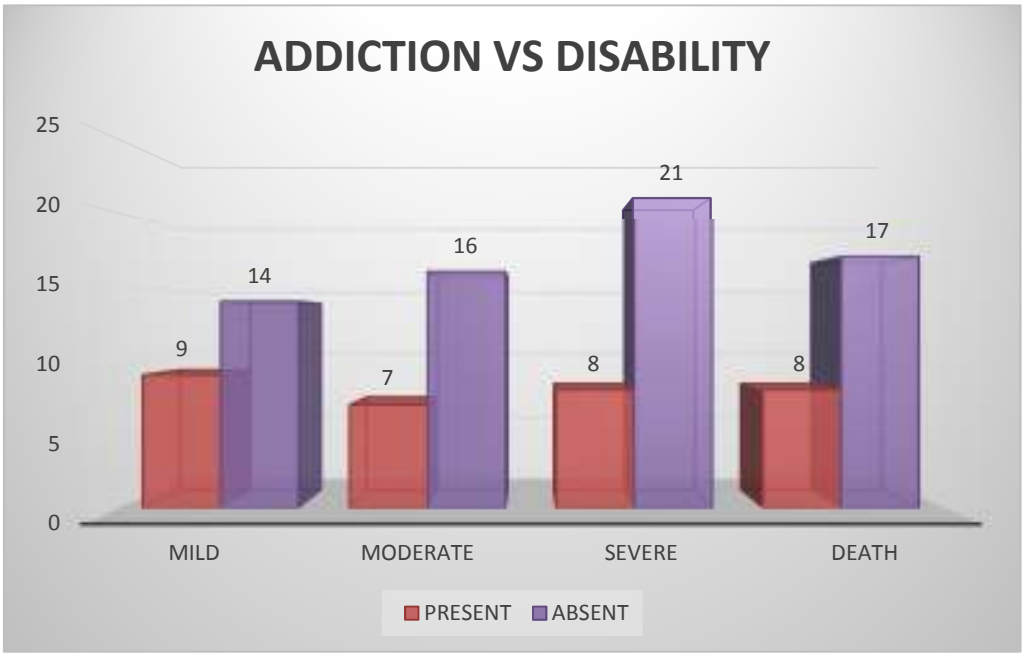


TABLE NO 15:TYPE OF LESION

TYPE OF LESION	NO OF PATIENTS	PERCENTAGE
MCA INFARCT	52	52%
MULTI INFARCT	19	19%
POST CIRCULATION STROKE	4	4%
LACUNAR INFARCT	25	25%

CHART NO 14

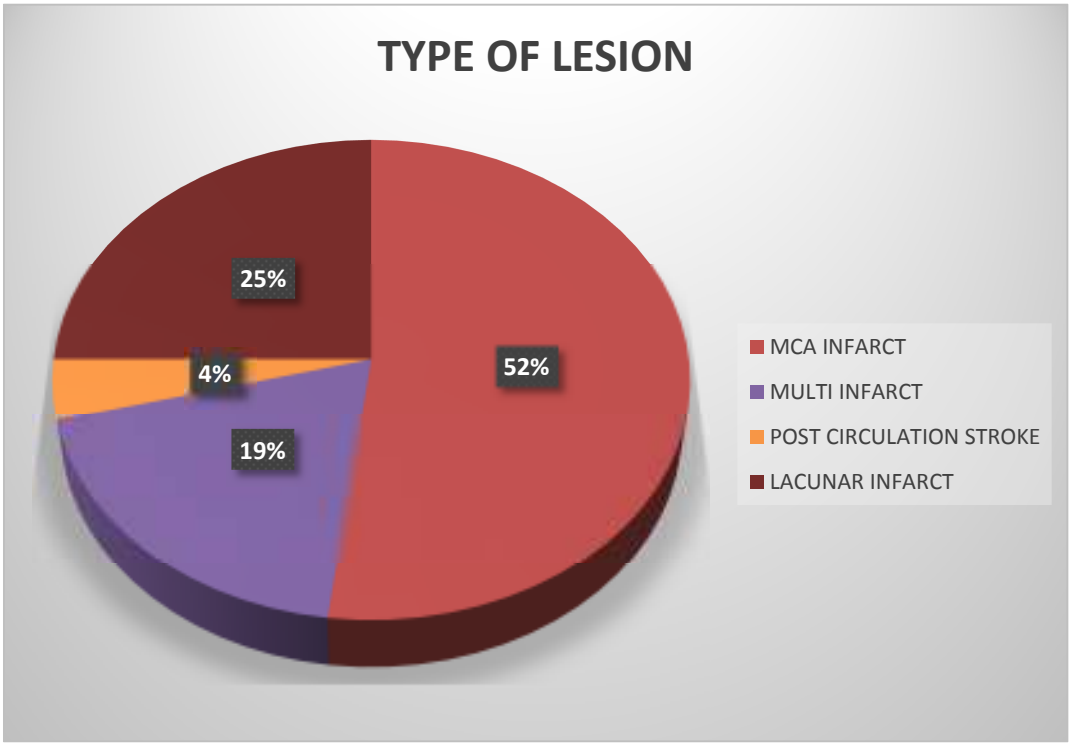


TABLE NO 16: DISABILITY VS TYPE OF LESION

DISABILITY (MRS SCORE)	TYPE OF LESION			
	MCA INFARCT	MULTI INFARCT	POSTERIOR CIRC STROKE	LACUNAR INFARCT
MILD	14	3	0	6
MODERATE	9	6	2	6
SEVERE	14	7	0	8
DEATH	15	3	2	5
KRUSKAL WALLIS TEST				
P VALUE - 0.509				
NON SIGNIFICANT				

CHART NO 15

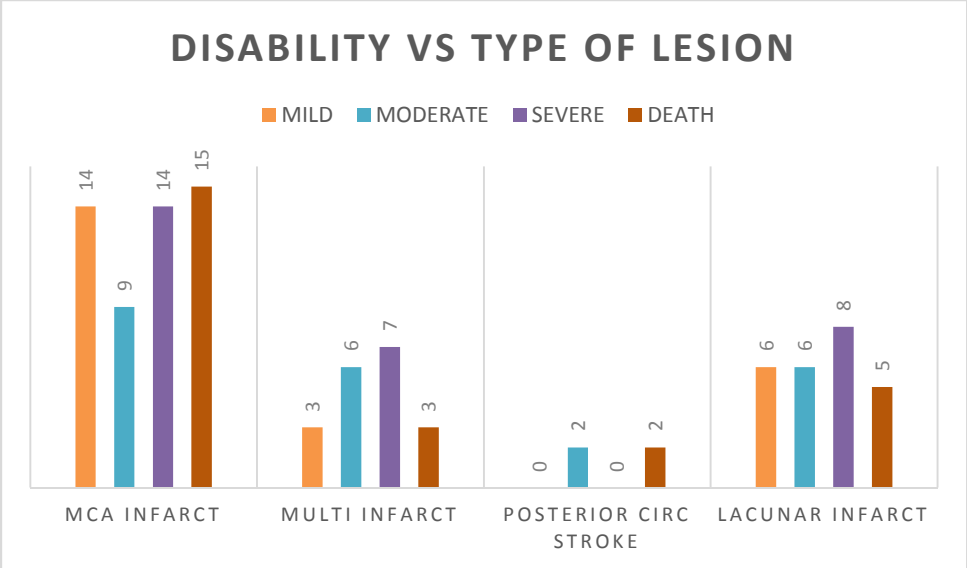


TABLE NO 17:GLASGOW COMA SCALE ON PRESENTATION

GLASGOW COMA SCALE	NO OF PATIENTS	PERCENTAGE
MILD (12-15)	12	12%
MODERATE (9-12)	45	45%
SEVERE (<9)	43	43%

CHART NO 16

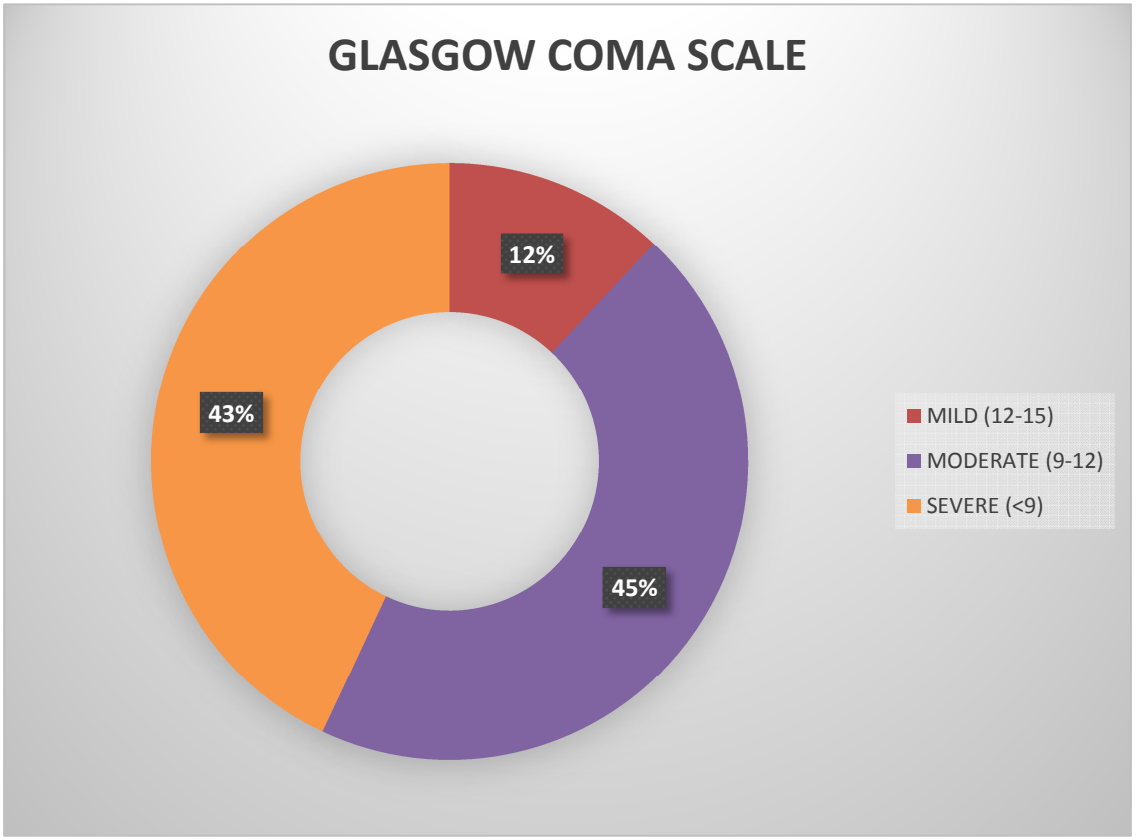


TABLE NO 18: DISABILITY VS GLASGOW COMA SCALE

DISABILITY (MRS SCORE)	GLASGOW COMA SCALE		
	MILD	MODERATE	SEVERE
MILD	11	12	0
MODERATE	1	18	4
SEVERE	0	15	14
DEATH	0	0	25
KRUSKAL WALLIS TEST			
P VALUE - 0.001			
SIGNIFICANT			

CHART NO 17

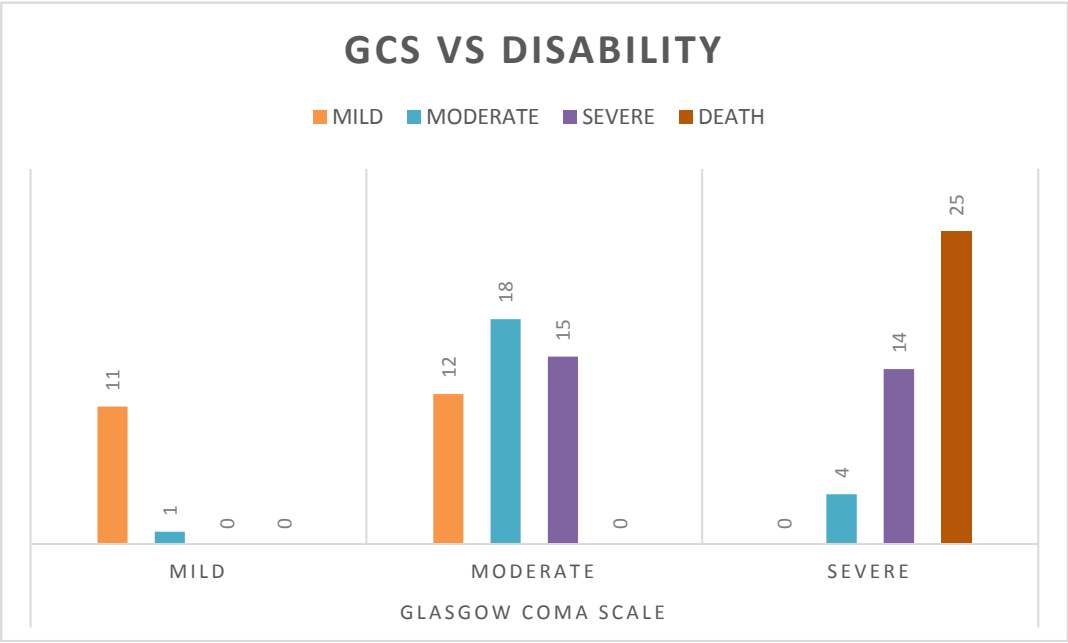


TABLE NO 19:SCANDINAVIAN STROKE SCALE(SSS) SCORE ON PRESENTATION

SCANDINAVIAN STROKE SCALE	NO OF PATIENTS	PERCENTAGE
MILD (43-58)	6	6%
MODERATE (26-42)	36	36%
SEVERE (0-25)	58	58%

CHART 18

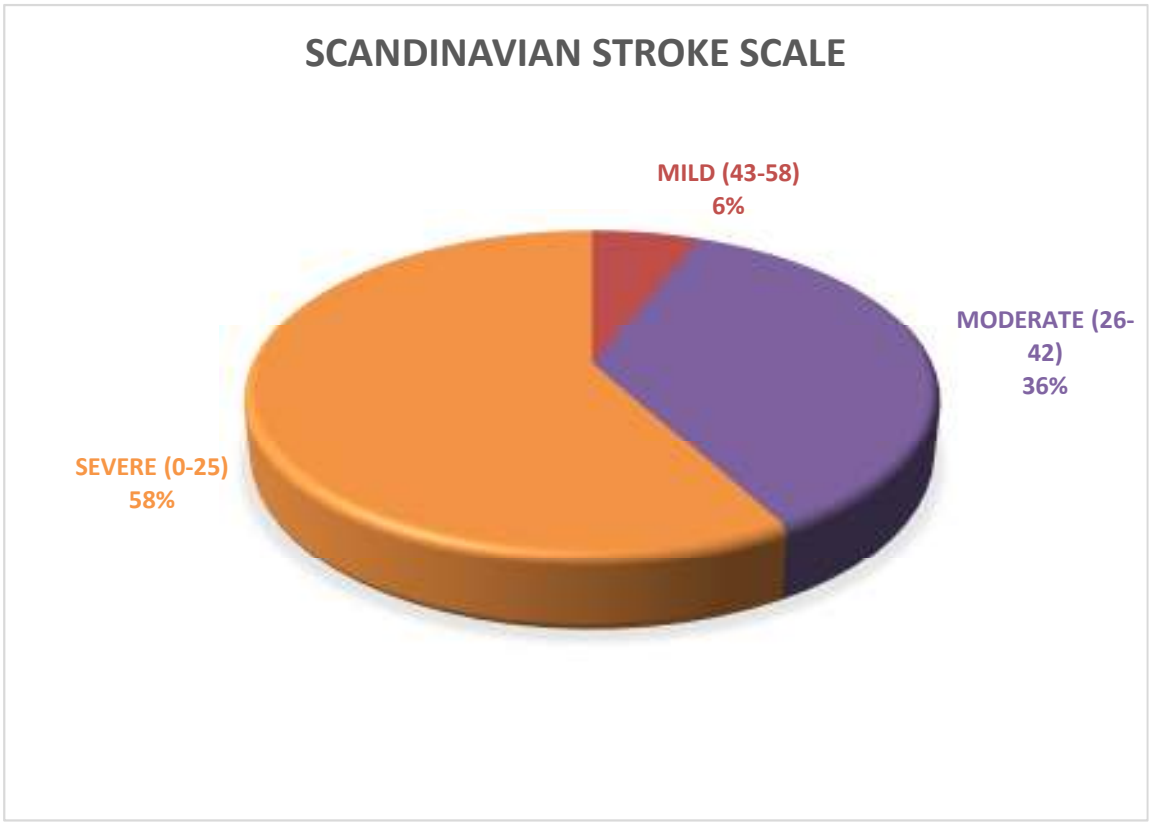
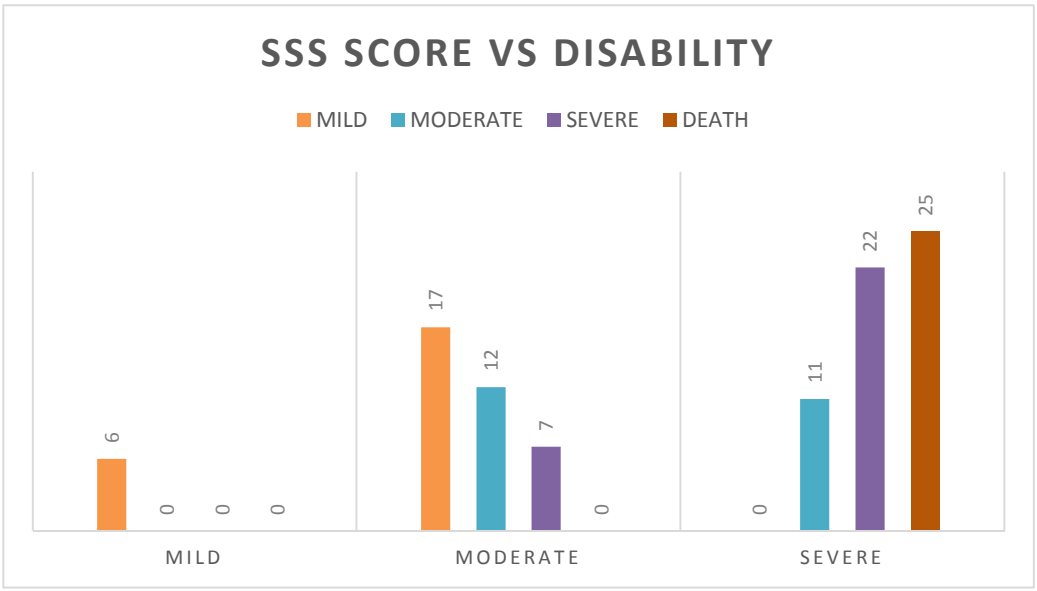


TABLE 20: DISABILITY VS SSS SCORE

DISABILITY (MRS SCORE)	SCANDINAVIAN STROKE SCALE		
	MILD	MODERATE	SEVERE
MILD	6	17	0
MODERATE	0	12	11
SEVERE	0	7	22
DEATH	0	0	25
KRUSKAL WALLIS TEST			
P VALUE - 0.001			
SIGNIFICANT			

CHART NO 19



18

TABLE NO 21: DISABILITY VS SERUM ALBUMIN

DISABILITY (MRS SCORE)	SERUM ALBUMIN	
	MEAN	SD
MILD	4.24	0.27
MODERATE	4.05	0.42
SEVERE	3.31	0.65
DEATH	2.9	0.51
ANOVA		
P VALUE - 0.001		
SIGNIFICANT		

CHART NO 20

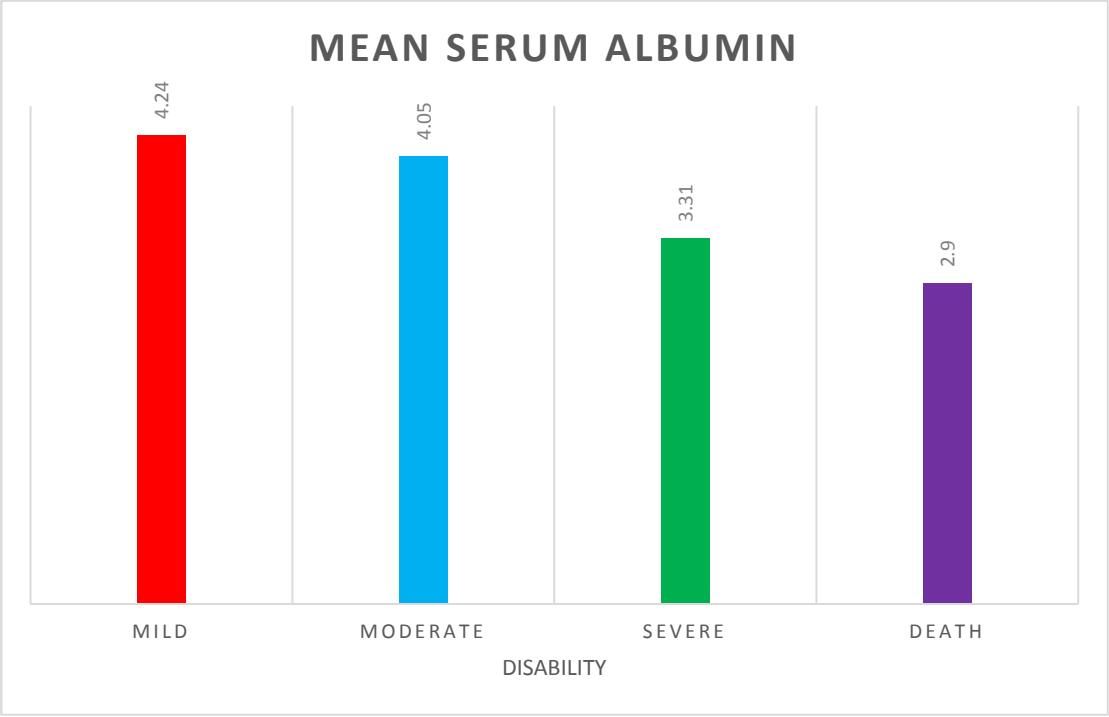


TABLE NO 22: SSS SCORE VS SERUM ALBUMIN

SCANDINAVIAN STROKE SCALE	SERUM ALBUMIN	
	MEAN	SD
MILD	4.2	0.45
MODERATE	3.9	0.65
SEVERE	3.34	0.68
ANOVA		
P VALUE - 0.001		
SIGNIFICANT		

CHART NO 21

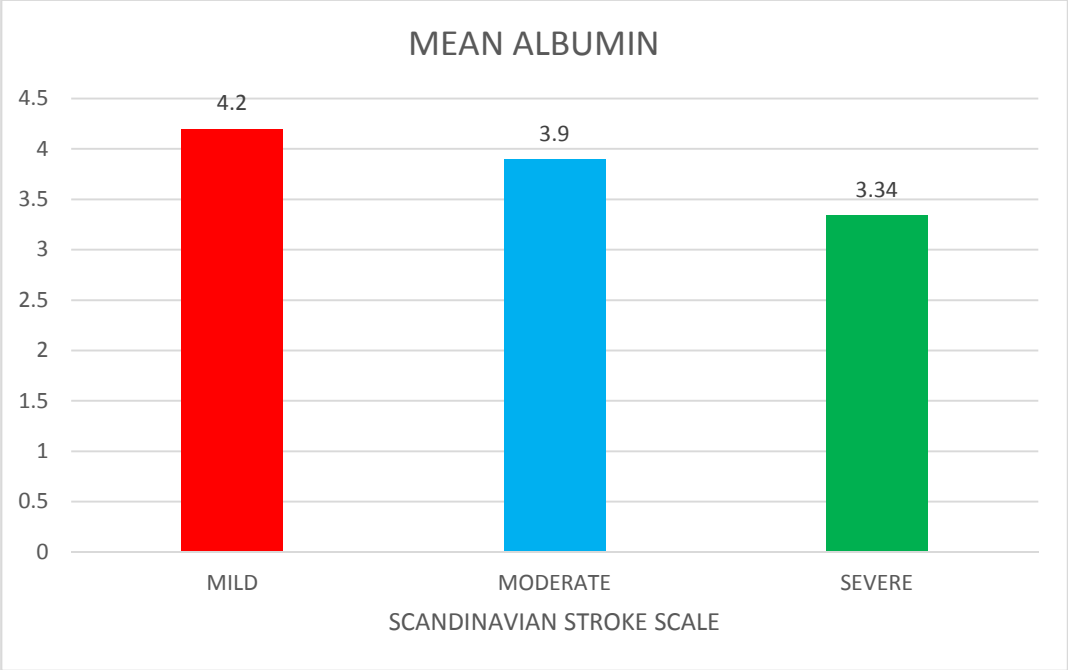


TABLE NO 23: GLASGOW COMA SCALE VS SERUM ALBUMIN

GLASGOW COMA SCALE	SERUM ALBUMIN	
	MEAN	SD
MILD	4.23	0.18
MODERATE	3.83	0.62
SEVERE	3.15	0.66
ANOVA		
P VALUE - 0.001		
SIGNIFICANT		

CHART NO 22

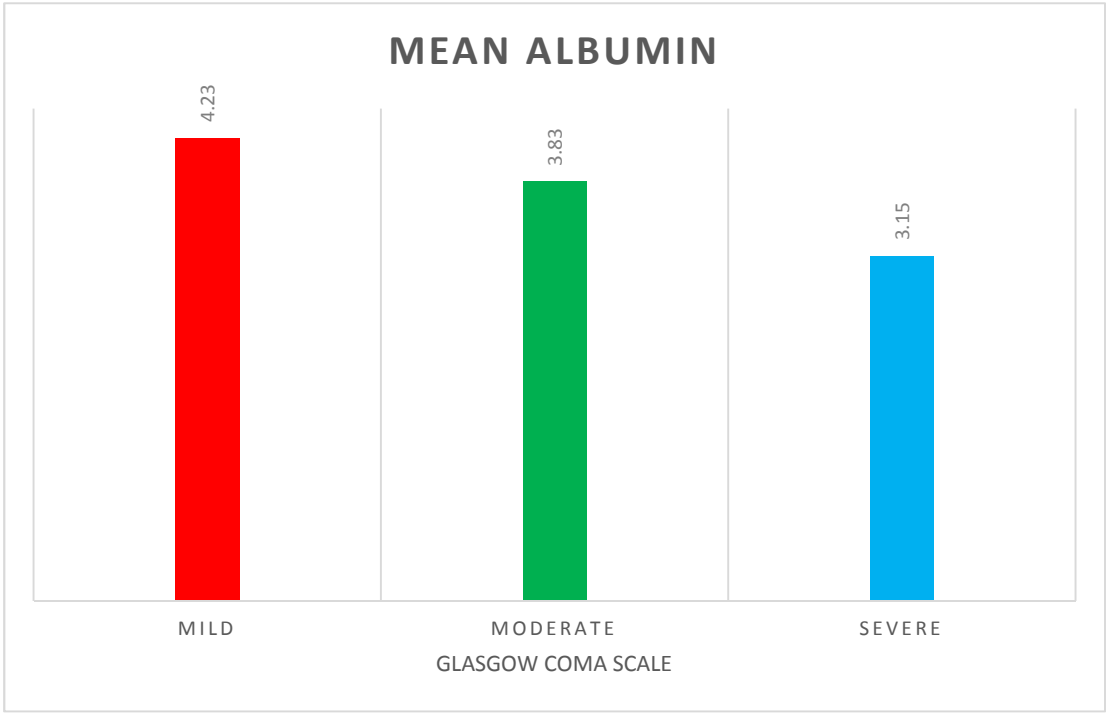


TABLE NO 24: TYPE OF LESION VS SERUM ALBUMIN

TYPE OF LESION	SERUM ALBUMIN	
	MEAN	SD
MCA INFARCT	3.57	0.69
MULTI INFARCT	3.8	0.49
POST CIRCULATION STROKE	3.2	0.95
LACUNAR INFARCT	3.5	0.9
ANOVA		
P VALUE - 0.402		
NON SIGNIFICANT		

CHART NO 23

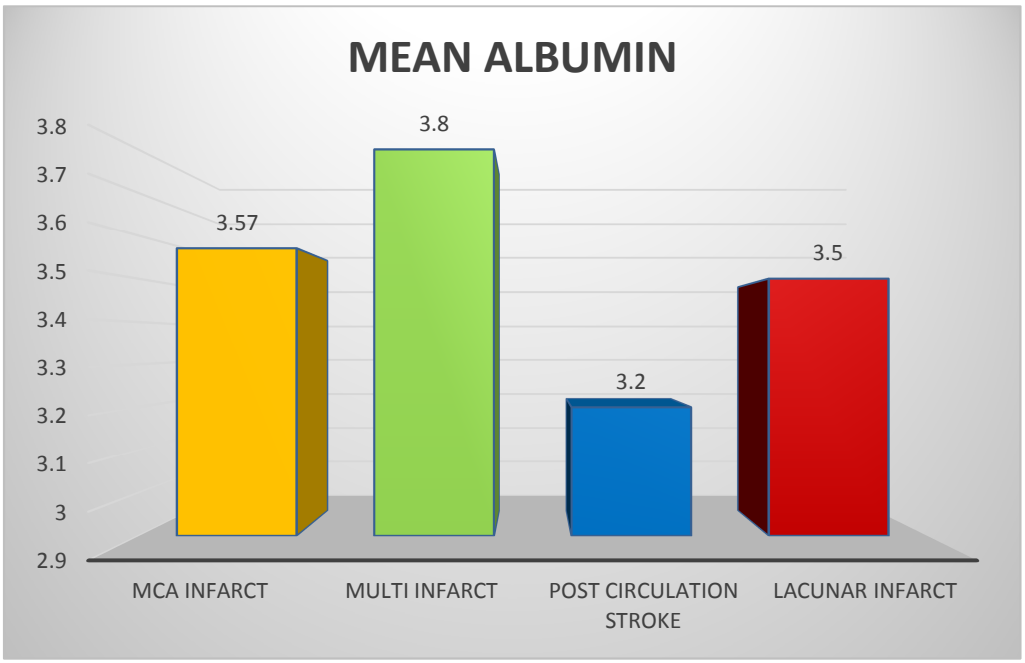
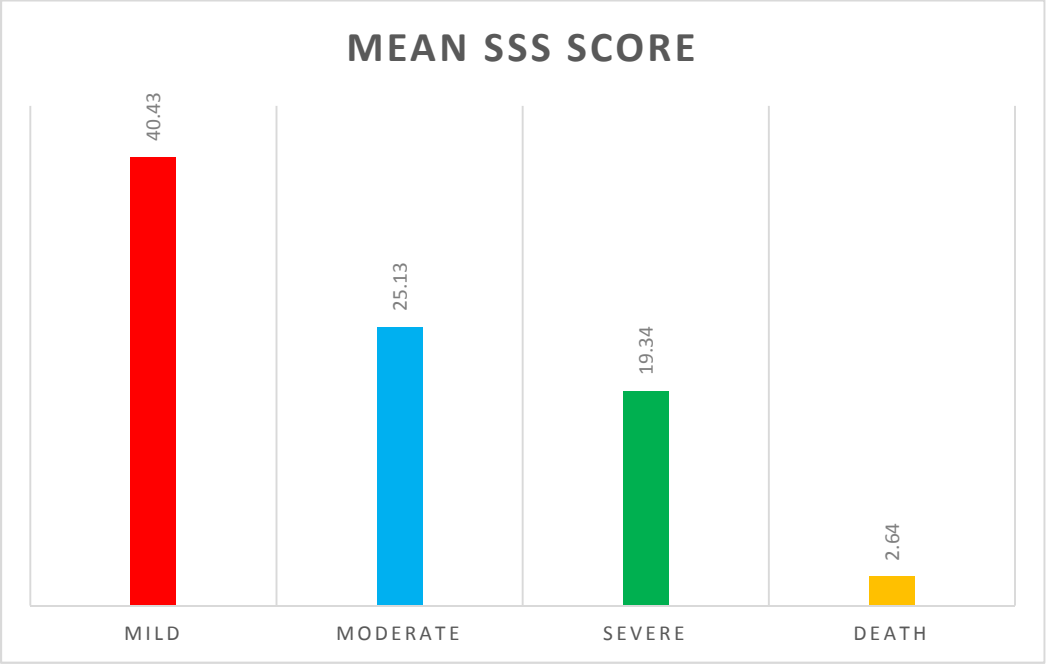


TABLE NO 25: DISABILITY VS SSS SCORE

DISABILITY (MRS SCORE)	SCANDINAVIAN STROKE SCALE	
	MEAN	SD
MILD	40.43	4.99
MODERATE	25.13	7.11
SEVERE	19.34	9.73
DEATH	2.64	2.13
ANOVA		
P VALUE - 0.001		
SIGNIFICANT		

CHART NO 24



SUMMARY

OBJECTIVE

1. To study whether serum albumin is a good prognostic indicator of acute ischemic stroke using modified rankin scale at 3 months follow up of patients admitted in general medicine ward, Coimbatore medical college hospital.

2. To identify other clinical and biochemical factors affecting the prognosis of acute ischemic stroke as measured by modified rankin scale at 3 months follow up.

METHODOLOGY

Patients admitted with first instance of ischemic stroke prsenting within 72 hours were screened and selected based on them satisfying the inclusion criteria after undergoing the customary investigations.

Those falling under the exclusion criteria were filtered out to end up with a pool of 100 patients.

Scandinavian stroke scale was used to assess the severity of stroke at the time of admission.

Serum albumin was calculated at the time of admission.

Functional status was assessed with the help of modified rankin scale at the end of 90 days, either by direct interview or over the phone.

Statistical analysis was carried out to find if there existed a statistically significant association between the serum albumin on admission and the functional status at 90 days. Other variables were also assessed for significance.

DISCUSSION

Albumin is a molecule with multifaceted action on various systems in the body. Neuroprotective effects of albumin have been well documented in animal studies. Studies have been conducted in the western population regarding the usefulness of serum albumin as an indicator of prognosis in ischemic stroke. There are few Indian studies in this regard.

In our study, 56% were male, and the ramainder female, in keeping with the other studies on stroke undertaken in our population

Majority of patients were in the 51-60 year age group, constituting 24% of the total patients. The mean age of 57.66±12.4, the oldest being 85 years old the youngest 27 years. There was no corelation between the age and serum albumin.

The major comorbidity that contributed to ishemic stroke in our study was systemic hypertension (57%), while diabetes constituted 27% of the total, while 18% had both. There was no significant association between serum albumin and comorbidities.

The other riskfactors were coronary artery disease, dyslipidemia and rheumatic heart disease (RHD). RHD contributed to the majority of stroke less than 35 years.

Smoking and alcohol intake was found in 32% of the subjects.

Majority of subjects had lesion in the MCA territory (52%) in keeping with the national and international studies.

GCS vs ALBUMIN

The association between GCS and albumin was found to be significant(p value<0.05) using the anova test. The mean albumin in those with GCS>13 was 4.23 mg/dl while those for GCS< 9 was 3.15 mg/dl.

SSS AND ALBUMIN

The association between SSS and albumin had a significant association with a p value<0.05. Hence proving that there was a positive corelation between the SSS score at admission and the serum albumin. The mean albumin in patients with mild impairment was 4.2 mg/dl, while in those with severe impairment was 3.34 mg/dl.

MRS AND ALBUMIN

Using anova test, the association between MRS and serum albumin had a p value<0.05 which was significant. Hence there was a negative correlation between serum albumin at admission with the MRS score at 90 days. The mean albumin level in subjects with mild diability was 4.2 mg/dl, as opposed to 3.31 mg/dl in patients with severe disability, and 2.9 mg/dl in patients who died. The higher the serum albumin level, the lower the MRS score, hence better the outcome at 90 days.

SSS SCORE AND MRS SCORE

There was a strong negative correlation between the SSS score at admission and the MRS score at 90 days. This entails that higher the SSS score, lower the MRS score hence more the disability at 90 days.

CONCLUSION

- There was no significant association of serum albumin with either sex or age
- Majority of subjects were in the 50-60 year age group
- Hypertension and diabtetes were the major risk factors
- Serum albumin has a significant association with the severity as well as the prognosis of stroke

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DEPARTMENT OF GENERAL MEDICINE, COIMBATORE MEDICAL COLLEGE HOSPITAL

PROFORMA

A STUDY OF SERUM ALBUMIN LEVEL AS A PROGNOSTIC INDICATOR OF ACUTE ISCHEMIC STROKE

CASE NO:

NAME:

AGE/SEX:

IP NUMBER:

ADDRESS:

PHONE NUMBER:

PRESENTING COMPLAINTS

- WEAKNESS
- GIDDINESS
- SEIZURE
- UNRESPONSIVENESS
- UNSTEADINESS OF GAIT
- DEVIATION OF ANGLE OF MOUTH

DURATION OF SYMPTOMS:

H/O FEVER/TRAUMA

PAST HISTORY

- PRIOR STROKE
- DIABETES MELLITUS
- HYPERTENSION
- CARDIAC DISEASES
- EPILEPSY
- TUBERCULOSIS

TREATMENT HISTORY:

FAMILY HISTORY:

ADDICTIONS:

VITALS:

- PULSE-RATE AND RHYTHM
- BLOOD PRESSURE
- RESPIRATORY RATE
- TEMPERATURE

GENERAL EXAMINATION

SYSTEMIC EXAMINATION

CENTRAL NERVOUS SYSTEM

- HIGHER MENTAL FUNCTION: CONSCIOUSNESS

  ORIENTATION

  SPEECH

- CRANIAL NERVES
- MOTOR SYSTEM: TONE

  POWER

  REFLEXES

- SENSORY SYSTEM
- CEREBELLAR SIGNS
- MENINGEAL SIGNS
- GLASGOW COMA SCALE- E V M TOTAL SCORE: /15
- SCANDINAVIAN STROKE SCALE SCORE:

CARDIOVASCULAR SYSTEM

- APEX BEAT
- HEART SOUNDS
- MURMURS

RESPIRATORY SYSTEM

- BREATH SOUNDS
- ADDED SOUNDS

GASTROINTESTINAL SYSTEM

- ANY TENDERNESS
- LIVER SPAN
- SHIFTING DULLNESS

INVESTIGATIONS

- COMPLETE HEMOGRAM
- RANDOM BLOOD SUGAR
- BLOOD UREA
- SERUM CREATININE
- LIVER FUNCTION TEST
- LIPID PROFILE
- SERUM PROTEINS: TOTAL:

  ALBUMIN:
- URINE ROUTINE EXAMINATION: ALBUMIN:

  SUGAR:

  CAST:

  CELLS:
- ECG:
- CT- BRAIN:
- MODIFIED RANKIN SCALE SCORE (ON THE 90^{TH} DAY):

ANNEXURE-II

CONSENT FORM (ENGLISH)

I have come to know that Dr. M.MOHAMED FAIZAL BASHEER, Postgraduate in the Department of General Medicine is conducting a study on the topic, "A STUDY OF 100 CASES OF PANCYTOPENIA: A CLINICO-HEMATOLOGICAL CORRELATION".

I understand that I will not have to suffer any harmful consequences as a result of the study nor will I have any financial constraints. It is understood that blood will be collected from me/bone marrow aspiration or trephine biopsy will be done for me for the purpose of conducting this study. I also understand that I can withdraw myself from this study at any point of time and by doing so it will not affect my treatment in any manner. Understanding all these, I wholeheartedly agree to take part in this study.

Signature

Name of the patient:

Signature

Name of the doctor:

Place:

Date:

ஒப்புதல் படிவம்

பெயர் :

வயது :

பாலினம் :

முகவரி :

கோவை அரசு மருத்துவக் கல்லூரி மருத்துவமனையில் மரு. **ஆகாஷ் சோழக்காடு** தலைமையில் நடைபெறும் இந்த ஆய்வில் எனது முழுஉடல் மற்றும் இரத்தப் பரிசோதனை செய்து கொள்ள முழு மனதுடன் சம்மதிக்கிறேன். என்னைப் பற்றிய விவரங்களை பாதுகாப்புடன் இந்த ஆய்வில் வெளியிட ஆட்சேபணை இல்லை என்று தெரிவித்துக் கொள்கிறேன். நான் எந்த நேரத்திலும் ஆய்வில் இருந்து விலக்கிக் கொள்ளும் உரிமை உண்டு என்று அறிவேன்.

இடம் கையொப்பம்/கைரேகை

தேதி

MASTER CHART

S.NO	NAME	AGE	SEX	SHT	T2DM	OTHERS	ADDICTION	LESION	GCS	S.ALBUMIN	SSS SCORE	MRS SCORE	DISABILITY
1	VANAJA	55	F	Y	N	N	S	1	5	4.2	6	6	DEATH
2	SEETHALAKSHMI	70	F	Y	N	N	N	4	14	4.2	30	4	MODERATE
3	BALASUBRAMANIAM	53	M	Y	Y	C,D	S	2	11	3.5	32	4	MODERATE
4	THEVASUMANI	35	F	N	Y	N	N	2	5	4.3	10	5	SEVERE
5	MANOHARAN	72	M	Y	N	D	S	1	9	3	14	5	SEVERE
6	VISWANATHAN	66	M	N	N	N	N	1	6	2.5	4	6	DEATH
7	KANDHASAMY	50	M	Y	N	N	L	2	12	4.4	26	4	MODERATE
8	ASHOK	29	M	N	N	R	N	2	9	4.1	20	5	SEVERE
9	ANMBROSE	55	M	N	N	N	S,L	1	5	3.6	2	6	DEATH
10	CHELLAMUTHU	68	M	Y	N	N	N	1	7	2.7	12	6	DEATH
11	RANGASAMY	72	M	N	Y	D	S	1	12	4.5	46	1	MILD
12	VENU	60	M	N	N	N	N	2	13	4	48	2	MILD
13	MURALIDHARAN	38	M	N	N	D	N	1	5	3	2	6	DEATH
14	THANGAPANDI	63	M	N	N	N	N	1	15	4.2	49	1	MILD

15	SUBBAIAH	78	M	Y	N	N	S	1	9	4.7	15	4	MODERATE
16	CHELAPPAN	47	M	N	N	D	N	1	9	3	15	5	SEVERE
17	MANOHARI	55	F	Y	N	N	N	1	5	2.7	2	6	DEATH
18	RAJAN	64	M	Y	N	N	L	1	8	3.4	10	5	SEVERE
19	RAMIAH	68	M	Y	N	D	N	1	9	4	11	5	SEVERE
20	KARUPPAN	65	M	N	N	D	N	1	14	4.3	42	3	MILD
21	GUNASEELAN	40	M	Y	N	N	S	3	11	3.8	24	4	MODERATE
22	SUBBAN	62	M	Y	N	N	N	1	12	3.4	44	2	MILD
23	VASUNDHARA	60	F	Y	N	N	N	1	5	2.4	2	6	DEATH
24	VANAJA	45	F	N	N	N	S	3	4	2.6	2	6	DEATH
25	NETAJI	42	M	N	Y	N	N	1	9	4.1	15	4	MODERATE
26	NAGAVALLI	52	F	Y	Y	C,D	N	1	6	4.7	16	5	SEVERE
27	LAKSHMI	85	F	Y	N	D	N	1	9	4.2	31	4	MODERATE
28	MASILLAMANI	46	M	Y	Y	N	L	4	5	2.8	2	6	DEATH
29	PAPPATHY	60	F	N	Y	N	N	1	8	4	31	4	MODERATE
30	CHINNAMANI	55	F	Y	Y	N	N	4	7	4.5	30	4	MODERATE
31	PALANISAMY	60	M	N	N	N	S	4	12	4.4	41	2	MILD
32	THIRUMAN	72	M	N	N	N	S	1	13	4.5	39	3	MILD
33	ARUMUGAM	65	M	Y	Y	C	N	4	15	4.6	46	1	MILD
34	PONNATHAL	52	F	N	N	N	L	4	8	3	15	5	SEVERE

35	POUNTHAI	55	F	Y	N	N	S	4	9	2.1	42	5	SEVERE
36	CHANDRA	37	F	N	N	N	N	1	5	2.8	2	6	DEATH
37	HASEENA	70	F	N	N	N	N	1	5	3.2	2	6	DEATH
38	KALAVATHY	44	F	Y	N	N	N	1	6	3	2	6	DEATH
39	PATHUMMA	80	F	Y	Y	C,D	N	2	9	3.1	41	5	SEVERE
40	BABU	38	M	Y	N	N	S	4	6	3.6	2	6	DEATH
41	AMSAVENI	39	F	N	Y	N	N	4	9	4.8	15	4	MODERATE
42	VICTOR	56	M	Y	Y	N	S,L	1	5	3.4	2	6	DEATH
43	AYSHABEEVI	80	F	N	N	N	N	1	5	2.6	2	6	DEATH
44	MOHD YUSUF	72	M	N	N	N	S	1	10	4.1	40	3	MILD
45	SARASWATHY	52	F	Y	N	N	N	1	9	4.1	16	4	MODERATE
46	VAIRAMUTHU	43	M	Y	N	N	N	4	7	3.2	34	4	MODERATE
47	VIVEKANAND	39	M	Y	N	N	L	4	12	4.6	33	4	MODERATE
48	SURESH KUMAR	42	M	N	N	N	N	4	11	2.8	29	5	SEVERE
49	PHILOMINA	65	F	Y	Y	N	N	4	9	4.5	39	1	MILD
50	PHILIP	75	M	Y	N	N	N	4	7	3.3	19	5	SEVERE
51	SULAIMAN	60	M	Y	N	N	N	1	6	3.4	14	5	SEVERE
52	DHANDAPANI	60	M	Y	Y	N	N	1	5	2.6	2	6	DEATH
53	BABU	43	M	N	Y	N	S	1	9	4	34	4	MODERATE
54	MOORTHY	42	M	N	N	N	N	1	9	4.1	21	4	MODERATE

55	MURUGAN	50	M	Y	Y	N	N	4	8	3.9	20	4	MODERATE
56	VALLIYAMMAL	72	M	N	N	N	N	3	5	2.2	2	6	DEATH
57	MARATHAL	72	F	Y	Y	C	S	1	6	3.6	4	5	SEVERE
58	ALAGIRI	45	M	N	N	N	N	1	9	4	10	5	SEVERE
59	MUTHAIAH	75	M	Y	N	N	S	2	10	4.2	30	5	SEVERE
60	PARVATHY	62	F	Y	N	N	N	2	12	4.2	36	4	MODERATE
61	SUNDAR	42	M	Y	N	N	N	2	5	3	2	6	DEATH
62	MANIKYAM	45	F	Y	N	N	N	1	5	2.8	2	6	DEATH
63	VANALAKSHMI	47	F	N	N	N	N	1	11	4.1	29	3	MILD
64	MARUTHACHALAM	80	M	Y	N	N	N	4	12	4.6	33	2	MILD
65	VANI	62	F	N	N	N	N	2	9	3.6	20	5	SEVERE
66	DURAISAMY	44	M	N	N	N	N	4	8	3.4	12	5	SEVERE
67	PRATHEEKSHA	27	F	N	N	R	N	2	10	4.1	23	4	MODERATE
68	JAHANGIR	66	M	N	N	N	S	1	11	4.2	29	3	MILD
69	MADHUBALA	44	F	N	Y	N	N	1	9	3.7	20	4	MODERATE
70	MUTHUSELVAN	56	M	N	N	N	N	2	9	3.8	15	4	MODERATE
71	MANIVASAGAM	55	M	N	Y	C	N	4	5	2.6	2	6	DEATH
72	SARANYA	45	F	Y	N	N	N	2	10	4	26	4	MODERATE
73	ZUBEIDA	44	F	Y	Y	N	S	2	13	4.1	38	3	MILD
74	KARUPPUSAMY	83	M	Y	N	C	S,L	4	9	3.1	14	5	SEVERE

75	SANKARAPPAN	60	M	Y	N	N	N	2	6	4	24	5	SEVERE
76	SELVI	38	F	N	N	D	N	1	6	3.4	14	5	SEVERE
77	KARUPASAMY	64	M	Y	N	N	N	1	10	3.1	30	4	MODERATE
78	KANDHASAMY	48	M	Y	Y	N	N	1	13	4.2	39	3	MILD
79	SUBBULAKSHMI	58	F	Y	N	N	N	1	9	3.1	32	5	SEVERE
80	MANOHARI	83	F	Y	Y	C	S	4	5	2.4	2	6	DEATH
81	PAPPATHY	85	F	Y	N	N	N	1	6	2.1	4	5	SEVERE
82	KALIAMMAL	60	F	Y	Y	N	N	4	4	2.2	2	6	DEATH
83	KALPANA	41	F	Y	N	N	N	1	12	4	41	3	MILD
84	KUMAR	39	M	Y	N	N	S	1	7	3.7	24	5	SEVERE
85	SABIYABEE	66	F	N	N	N	S	3	9	4.2	21	4	MODERATE
86	MANORANJITHAM	76	F	Y	N	N	N	1	11	2.8	29	5	SEVERE
87	PASUPATHY	60	M	N	N	N	N	2	5	3	2	6	DEATH
88	DEVASENA	45	F	N	Y	N	N	4	8	2.1	30	5	SEVERE
89	KANNAMAL	82	F	Y	N	N	S	4	12	4.6	40	3	MILD
90	BINDU	57	F	Y	Y	N	N	1	14	4.4	41	3	MILD
91	MANICKAM	85	M	Y	N	N	S	1	12	4.1	39	3	MILD
92	LAKSHMI	40	F	N	N	N	N	4	12	4	41	3	MILD
93	NANJAMMAL	70	F	Y	N	N	N	1	10	3	16	5	SEVERE
94	PAPPATHY	66	F	N	N	N	N	2	4	4	2	6	DEATH

95	VENDA	72	F	Y	Y	N	N	1	14	4.5	43	2	MILD
96	JOSEPH	75	M	N	N	N	L	1	5	2.7	2	6	DEATH
97	SANKAR	60	M	N	N	N	N	2	9	2.8	18	5	SEVERE
98	RANGAMMAL	65	F	Y	N	N	N	4	6	3	24	5	SEVERE
99	AMSAVENI	38	F	N	N	N	N	1	15	4.2	42	2	MILD
100	BALASUBRAMANIAM	67	M	Y	Y	N	S	2	13	4.1	41	2	MILD

KEY TO MASTER CHART

1- MCA INFARCT

2- MULTI-INFARCT

3- PCA/POSTERIOR CIRCULATION STROKE

4- LACUNAR STROKE

C- CORONARY ARTERY HEART DISEASE

D-DYSLIPIDEMIA

R-RHEUMATIC HEART DISEASE

S-SMOKING

L-ALCOHOL

Y-YES

N-NIL

SEVERITY GRADING	**MILD**	**MODERATE**	**SEVERE**	**DEATH**
MRS	0-3	4	5	6
SSS	43-58	26-42	0-25	-